Statistical Analysis Plan

Sponsor:	Arcutis Biotherapeutics, Inc.
Protocol Title:	A Phase 1/2b, Multiple Dose and 12-Week, Parallel Group, Double Blind, Dose Ranging, Vehicle-Controlled Study of the Safety and Efficacy of ARQ-252 Cream 0.1% and ARQ-252 Cream 0.3% in Subjects with Chronic Hand Eczema
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Not applicable.

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
ANCOVA	analysis of covariance
ASA	American Statistical Association
ATC	anatomical therapeutic chemical
BID	twice daily
BMI	body mass index
BSA	body surface area
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
COVID-19	novel coronavirus disease-19
CS	clinically significant
CSR	clinical study report
ECG	Electrocardiogram
eCRF	electronic case report form
EM	expectation-maximization
EMA	European Medicines Agency
FDA	Food and Drug Administration
HECSI	Hand Eczema Severity Index
ICH	International Conference on Harmonisation
IGA	investigator global assessment
IP	investigational product
IRT	interactive response technologies
ITT	intent-to-treat
LS	least-squares
MCMC	Markov-Chain Monte-Carlo
MedDRA	Medical Dictionary for Regulatory Activities
mTLSS	Modified Total Lesion Symptom Score

Abbreviation	Definition
NA	not applicable
NCS	not clinically significant
ND	nail dystrophy
NRS	numeric rating scale
PK	Pharmacokinetics
PMM	predictive mean modeling
PP	per protocol
QD	once daily
QOLHEQ	Quality of Life in Hand Eczema Questionnaire
RSS	Royal Statistical Society
SAE	serious adverse event
SAF	Safety
SAP	statistical analysis plan
SAS®	a software system used for data analysis
SD	standard deviation
SE	standard error
SOC	system organ class
TEAE	treatment emergent adverse event
TLFs	tables, listings, and figures
WHO-DDE	World Health Organization Drug Dictionary Enhanced
WI-NRS	Worst Itch – Numeric Rating Scale

1. OVERVIEW

This statistical analysis plan (SAP) describes the planned analysis and reporting for Arcutis Biotherapeutics, Inc. protocol number ARQ-252-205 (A Phase 1/2b, Multiple Dose and 12-Week, Parallel Group, Double Blind, Dose Ranging, Vehicle-Controlled Study of the Safety and Efficacy of ARQ-252 Cream 0.1% and ARQ-252 Cream 0.3% in Subjects with Chronic Hand Eczema), dated 30-June-2020 Amendment Version 2. Reference materials for this statistical plan include the protocol and the accompanying sample data collection documents. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH 1998). All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association (ASA 2018) and the Royal Statistical Society (RSS 2014), for statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc or unplanned, exploratory analysis performed will be clearly identified as such in the final CSR.

The statistical plan described hereafter is an *a priori* plan. It will be submitted to file before any unblinded inferential or descriptive analysis of data pertaining to Arcutis Biotherapeutics, Inc.'s study ARQ-252-205. Any amendments to this plan that occur after unblinding for an interim analysis will be performed by a study statistician who remains blinded to treatment codes and outcomes.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Study Objectives

2.1.1. Primary Objectives

The objectives of this study are as follows:

Phase 1 (Cohort 1):

- To assess the safety, tolerability, and pharmacokinetics (PK) of once daily (QD) application of ARQ-252 0.3% to both hands for 2 weeks in 6 subjects with chronic hand eczema

Phase 2b (Cohort 2):

- To assess the safety and efficacy of ARQ-252 cream 0.1% QD and ARQ-252 cream 0.3% QD and twice daily (BID), vs vehicle applied QD and BID for 12 weeks to subjects with chronic hand eczema

2.2. Study Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoint

Phase 1 (Cohort 1):

Not applicable.

Phase 2b (Cohort 2):

The primary endpoint of Cohort 2 is:

- The rate of an Investigator Global Assessment (IGA) score of "clear" or "almost clear" at Week 12

The primary estimand for the primary efficacy endpoint of this study is the odds of achieving IGA score of "clear" or "almost clear" (i.e., IGA success) at 12 weeks; that is, the ratio of the odds of achieving IGA success at 12 weeks ARQ-252 relative to the odds of success at 12 weeks of using a matching vehicle cream. In the course of the 12-week randomized treatment period, subjects may be exposed to possible known or unknown intercurrent events that could possibly affect the estimand, such as treatment discontinuation due to a specific adverse effect or perhaps a lack of effect. The "Treatment Policy Strategy" has been adopted for handling all known or unknown intercurrent events in this study. To this end, the ITT principle will serve as the analytical basis for interpreting the estimand. In other words, the odds ratio of achieving IGA success for ARQ-252 relative to vehicle at 12 weeks will be evaluated regardless of the occurrence of any such intercurrent event. This estimand shall be estimated using the Cochran-Mantel-Haenszel (CMH) approach and applies to the following treatment comparisons:

- ARQ-252 cream 0.3% BID versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.1% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream (all strengths and dose frequencies) versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% (all dose frequencies) versus vehicle cream (all dose frequencies)

2.2.1.2. Secondary Efficacy Endpoint(s)

Phase 1 (Cohort 1):

Not applicable.

Phase 2b (Cohort 2):

The secondary endpoints of Cohort 2 are:

- The rate of achievement of IGA of "clear" or "almost clear" PLUS at least a 2-point improvement from baseline at Weeks 2, 4, 8, 12, and 13
- The rate of achievement of at least a 2-point improvement from baseline at Weeks 2, 4, 8, 12, and 13
- Achievement of IGA of "clear" or "almost clear" at Weeks 2, 4, 8, and 13
- Change in IGA score at Weeks 2, 4, 8, 12, and 13 as compared to baseline
- Change and percent change in Worst Itch - Numeric Rating Scale (WI-NRS) pruritus score at Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 compared to baseline
- The rate of achievement of ≥4-point reduction from baseline in WI-NRS pruritus score at Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 in subjects with baseline WI-NRS pruritus score of at least 4
- Change and percent change in Hand Eczema Severity Index (HECSI) score at Weeks 2, 4, 8, 12, and 13 compared to baseline
- Achievement of HECSI-75
- Change and percent change in Pain Numeric Rating Scale (NRS) score from Baseline to Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13
- The rate of achievement of ≥4-point reduction from baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 4
- The rate of achievement of ≥3-point reduction from baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 3
- The rate of achievement of ≥2-point reduction from baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 2
- Change and percent change from baseline in overall Quality of Life in Hand Eczema Questionnaire (QOLHEQ) score at each study visit
- Percent body surface area (BSA) affected by disease and % change from baseline in BSA affected by disease at baseline, 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 13 weeks.

2.2.1.3. Exploratory Efficacy Endpoint(s)

Phase 2b (Cohort 2):

The exploratory endpoint of Cohort 2 is:

- Change from baseline in Nail Dystrophy at each visit.

2.2.2. Safety Endpoints

Phase 1 (Cohort 1):

The primary endpoint of Cohort 1 is safety, as measured by the incidence and severity of adverse events (AEs), changes in laboratory parameters, tolerability, and PK.

Phase 2b (Cohort 2):

The safety endpoints for Phase 2b (Cohort 2) will be the same as for Phase 1 (Cohort 1), i.e., as measured by the incidence and AEs, changes in laboratory parameters, tolerability, and PK.

3. OVERALL STUDY DESIGN AND PLAN

3.1. Overall Design

This is a phase 1/2b, multiple dose and 12-week, parallel group, double blind, dose ranging, vehicle-controlled study of the safety and efficacy of ARQ-252 cream 0.1% and ARQ-252 cream 0.3% in subjects with chronic hand eczema.

There are 2 cohorts of subjects:

- Cohort 1 is a multiple dose cohort in which subjects with chronic hand eczema will be assigned to ARQ-252 cream 0.3% QD x 2 weeks to be applied to both hands. Pharmacokinetics and tolerability will be evaluated.
- Cohort 2 is a parallel group, double blind, vehicle-controlled cohort in which subjects with chronic hand eczema will be randomized to ARQ-252 cream 0.3% QD, ARQ-252 cream 0.3% BID, ARQ-252 cream 0.1% QD, vehicle cream BID, or vehicle cream QD x 12 weeks to be applied to both hands. Safety and efficacy will be evaluated.

A total of approximately 6 evaluable subjects will be enrolled in Cohort 1, and a total of approximately 215 subjects will be enrolled in Cohort 2. After having met all inclusion criteria, and none of the exclusion criteria, subjects in Cohort 1 will be assigned treatment with ARQ-252 cream 0.3% QD at the Baseline visit; and subjects in Cohort 2 will be randomized in a 2:2:1:1:1 ratio (ARQ-252 0.3% QD, ARQ-252 0.3% BID, ARQ-252 0.1% QD, vehicle cream QD, or vehicle cream BID, respectively) and stratified by study site and IGA at baseline according to a computer-generated randomization list.

For subjects enrolled in Cohort 1, subject participation involves a minimum of 7 clinic visits including Screening, Baseline/Day 1, Day 2, Day 8, Day 15, Day 16, and Day 22. Subjects will be treated with investigational product (ARQ-252 cream 0.3% QD) for 2 weeks. The interval between the Screening and Baseline visits could be up to 4 weeks, therefore the anticipated maximum duration of subject participation is 7 weeks.

For subjects enrolled in Cohort 2, subject participation involves a minimum of 7 clinic visits including Screening, Baseline/Day 1, Week 2, Week 4, Week 8, Week 12, and Week 13. Subjects will be randomized to a treatment group and will be treated with investigational product for 12 weeks. The interval between the Screening and Baseline visits could be up to 4 weeks, therefore the anticipated maximum duration of subject participation is 17 weeks.

3.2. Sample Size and Power

Cohort 1 will include approximately 6 evaluable subjects, which is deemed adequate for the purpose of evaluating safety and PK before Cohort 2 commences.

There are approximately 215 subjects planned for Cohort 2. The primary statistical comparisons will be to assess the ARQ-252 cream 0.3% BID group versus the vehicle BID group, to assess the ARQ-252 cream 0.3% QD group versus the vehicle QD group, and to assess the ARQ-252 cream 0.1% QD group versus the vehicle QD group. A sample size of 55 per active arm and 28 per vehicle arm will provide approximately 85% power at the 2-sided 10% significance level to detect a difference in the rate of subjects attaining an IGA score of clear or almost clear (for each ARQ-252-treated group versus vehicle group within the same daily dosing frequency), assuming an active treatment response rate of 45% and a vehicle response rate of 15%. For testing each active arm of 55 subjects versus the combined vehicle arms of 56 subjects, this sample size provides over 90% power for the comparison of the rate of subjects attaining an IGA score of clear or almost clear. This is based on a 2-group X2 test of equal proportions (without continuity correction).

3.3. Study Population

Subjects will be adults (≥18 years of age) males or females with chronic hand eczema involving at least 0.3% BSA, with a minimum IGA of at least “Mild” (2) at baseline.

3.4. Treatments Administered

Cohort 1 will include approximately 6 evaluable subjects; all subjects are to receive ARQ-252 cream 0.3% QD.

Approximately 61 subjects will receive ARQ-252 cream 0.3% QD, approximately 61 subjects will receive ARQ-252 cream 0.3% BID, approximately 31 subjects will receive ARQ-252 cream 0.1% QD, approximately 31 subjects will receive matching vehicle cream QD, and approximately 31 subjects will receive vehicle cream BID. The randomization scheme will be 2:2:1:1:1 between these 5 treatment groups, stratified by study site and IGA at Baseline.

3.5. Method of Assigning Subjects to Treatment Groups

Phase 1 (Cohort 1)

Phase 1 (Cohort 1) is open label and all enrolled subjects will be assigned treatment with ARQ-252 cream 0.3% QD at the Baseline visit. Subjects will be enrolled at the Baseline visit after the Investigator confirms that the subject meets all eligibility criteria listed in the protocol. Enrollment will be documented by the completion of the Enrollment Notification Form.

Phase 2b (Cohort 2)

Phase 2b (Cohort 2) is randomized. Randomization will take place at the Baseline visit after the Investigator confirms that the subject meets all eligibility criteria listed in the protocol. Subjects will be randomly assigned to apply ARQ-252 0.3% QD, ARQ-252 0.3% BID, ARQ-252 0.1% QD, vehicle cream QD, or vehicle cream BID by an interactive response technology system (IRT).

Assignment of treatment arm will be made at a 2:2:1:1:1 ratio and stratified by study site and IGA at baseline according to a computer-generated randomization list. Kits containing tubes of investigational product will be assigned to each subject by the IRT system. A subject may receive more than one kit for the treatment period. The kits and tubes will be labeled with a unique number, *in a blinded manner.*

3.6. Blinding and Unblinding

Phase 1 (Cohort 1) is not blinded.

Phase 2b (Cohort 2) is double-blinded, therefore neither the subjects nor the Investigator and clinical personnel will be aware of which investigational product (ARQ-252 0.1% cream, ARQ-252 0.3% cream, or vehicle cream) an individual subject receives. The subjects, Investigator, and clinical personnel will be aware of whether study is to be applied once daily or twice daily.

In the event of a medical emergency where breaking the blind is required to provide medical care to the subject, the Investigator may obtain the treatment assignment directly from the IRT system for that subject. Refer to the current version of the IRT plan for details on unblinding. Treatment assignments should, however, remain blinded unless assignment knowledge is necessary to determine subject emergency medical care. The rationale for unblinding must be clearly explained in source documentation and on the CRF, along with the date on which the treatment assignment was obtained. The Investigator is requested to contact the Sponsor promptly in the event of any treatment unblinding.

Blinding of study treatment is critical to the integrity of this clinical trial and therefore, if a subject's treatment assignment is disclosed to the Investigator, the subject will have the study treatment discontinued. All subjects will be followed until study completion unless consent to do so is specifically withdrawn by the subject.

3.7. Schedule of Events

The schedule of events for Cohort 1 (Phase 1) is presented in Table 1, and the schedule of events for Cohort 2 (Phase 2a) is presented in Table 2.

Table 1: Cohort 1 (Phase 1)

Study Procedure	Screening	Baseline Day 1	PK Collection Day 2	Day 8	Week 2 Day 15	PK Collection Day 16	Week 3 Day 22
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Visit Window	**-4 Weeks**		**+/- 2 hrs**	**+/-1 day**	**+/- 1 day**	**+/- 2 hrs**	**+/- 3 days**
Informed Consent	X						
Demographics	X						
Medical and Surgical History	X						
Physical examination[a]	X	X		X	X		X
I/E criteria	X	X					
Hematology, Serum Chemistries, Urine Analysis, TSH, T4[b]	X	X		X	X		X
Vital signs, weight, height[c]	X	X		X	X		X
Local tolerability assessment[d]		X		X	X		
BSA, IGA, HECSI[e]	X	X			X		
WI-NRS, NRS Pain[f]	X	→ Completed daily from Day 1-Day 15					
Urine pregnancy test[g]		X		X	X		X
Serum pregnancy test[g]	X						
Follicle-Stimulating Hormone (FSH)[h]	X						
Resting 12-lead ECG	X				X		
PK sampling[i]		X	X	X	X	X	
IP application in clinic[j]		X		X	X		
Dispense IP		X					
Weigh investigational product container[k]		X			X		
Dispense/review diary		X		X	X		
Adverse event assessment[l]	X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X

Footnotes from table above:

[a] Limited physical examination: skin, lungs, and heart only.

[b] All samples listed to be collected at Visits 1, 2, 4, 5, and 7. If Baseline visit occurs within 14 days of Screening, the Screening lab results may be utilized.

[c] Height to be measured only at Visit 2 (Day 1). Weight will be collected at Baseline, Visits 4, 5 and 7.

[d] Local tolerability assessments to be recorded prior to IP application for the Investigator assessment of skin irritation (Berger and Bowman skin irritation score) and 10-15 minutes post IP application for the subject's '0-3' burning/stinging assessment. **Note for investigator tolerability assessments: reactions at the site of IP application, which may occur post-Baseline, should be differentiated from the preexisting inflammation associated with the subject's chronic hand eczema.**

[e] BSA will be measured as the affected BSA for each side of each hand. Affected areas of the lateral aspects of the fingers and hands should be assigned to the palmar surface. IGA will be a 5-point scale ranging from clear (0) to severe (4). **IGA should be completed prior to other physician assessments and by the same Evaluator at each study visit.** HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 distinct hand anatomic areas by use of standard scales. The total HECSI score is based on a 4-point clinical sign severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the different affected hand anatomic area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area).

[f] Subjects will complete the WI-NRS pruritus assessment and NRS Pain assessment in the clinic during screening and then daily at home from the Baseline/Day 1 visit through the Day 15 visit.

[g] A serum pregnancy test will be administered to all females of child-bearing potential at Screening. A urine pregnancy test will be administered at Visits 2, 4, 5, and 7 to all females of childbearing potential. A negative result is required for continued participation in the study, and results must be available prior to dispensing of investigational product.

[h] FSH will be performed (if indicated) at Screening to confirm post-menopausal status.

[i] On the first day of dosing (Day 1), PK samples will be collected at 1, 2, 4, 6 (all +/- 10 mins) and 24 hours post-dose administration (Day 2, +/- 2 hours). On Day 15 (last dose application), PK samples will be collected pre-dose, 1, 2, 4, 6, (all +/- 10 mins) and 24 hours post dose administration (Day 16, +/- 2 hours). For 24-hour time points, subjects return to the clinic on the following day within 2 hours of the IP application time from the previous day for pre-dose PK plasma sample. A pre-dose PK sample will be taken at Day 8.

[j] Clinic personnel will apply assigned IP on Visits 2, 4 and 5 (Baseline, Day 8 and Day 15). Every tube should be weighed before and after IP application and weights recorded. For the 24-hour PK sampling time point the application of investigational product should occur after the PK sample has been collected.

[k] Subject should return with investigational product kit at each Visit. Every tube should be weighed before and after use and weights recorded when dispensed and returned.

[l] Any emergent AEs will be followed in the clinic for up to 1 month at the Investigator's discretion until resolved or otherwise judged as clinically stable

Table 2: Cohort 2 (Phase 2b)

Study Procedure	Screen	Baseline Day 1	Wk 2 Day 15	Wk 4 Day 29	Wk 8 Day 57	Wk 12 Day 85	Wk 13 Day 92
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Visit Window	-4 weeks		+/- 3 days	+/- 5 days	+/- 5 days	+/- 7 days	+/- 3 days
Informed consent	X						
Demographics	X						
Medical and surgical history	X						
Physical examination[a]	X	X				X	
Vital signs, height, weight[b]	X	X	X	X	X	X	X
I/E criteria	X	X					
Randomization		X					
Hematology, Serum Chemistries, UA, TSH/T4[c]	X	X		X	X	X	
Resting 12-lead ECG	X			X		X	
BSA, IGA, HECSI[d]	X	X	X	X	X	X	X
NRS pain, WI-NRS[e]	X	Completed daily from Day 1 to Week 13 Visit					
QOLHEQ[e]	X	X	X	X	X	X	X
Nail dystrophy assessment[f]		X	X	X	X	X	X
Local Tolerability Assessments[g]		X	X	X	X	X	
Optional Photography[h]		X	X	X	X	X	X
Urine pregnancy test[i]		X		X	X	X	X
Serum pregnancy test[i]	X						
Follicle-Stimulating Hormone (FSH)[j]	X						
PK sampling[k]		X		X		X	
IP application/Subject training in clinic[l]		X	X	X	X	X	
Dispense IP kit[m]		X	X	X	X	X	
Dispense/review diary		X	X	X	X	X	
Weigh IP tubes[n]		X	X	X	X	X	
Compliance calculation[o]		X	X	X	X	X	
Adverse event assessment[p]	X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X

Footnotes from table above:

[a] Limited physical examination: skin, lungs, and heart only

[b] Height will be collected at Visit 2 (Baseline/Day 1) only. Weight will be collected at Baseline, Weeks 4, 8 and 12.

[c] If Baseline visit occurs within 14 days of Screening, the Screening lab results may be utilized.

[d] BSA will be measured as the affected BSA for each side of each hand. Affected areas of the lateral aspects of the fingers and hands should be assigned to the palmar surface. IGA will be a 5-point scale ranging from clear (0) to severe (4). **IGA should be completed prior to other physician assessments and by the same Evaluator at each study visit.** HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 distinct hand anatomic areas by use of standard scales. The total HECSI score is based on a 4-point clinical sign severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the different affected hand anatomic area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area).

[e] Subjects will complete the WI-NRS pruritus assessment and NRS Pain assessment in the clinic during Screening and then daily at home from the Baseline/Day 1 visit until the Week 13 visit. QOLHEQ = Quality of Life in Hand Eczema Questionnaire will be completed at each visit.

[f] Assessment of nail dystrophy including Baseline identification of the nail with the worst dystrophy and measurement of the millimeters of normal appearing nail distal to the cuticle post Baseline. Sites participating in optional photography will obtain photos of nail with the worst dystrophy at Baseline/Day 1 and at subsequent visits.

[g] Local tolerability assessments to be recorded prior to IP application for the Investigator assessment of skin irritation (Berger and Bowman skin irritation score) and 10-15 minutes post IP application for the subject's '0-3' burning/stinging assessment. **Note for investigator tolerability assessments: reactions at the site of IP application, which may occur post-Baseline, should be differentiated from the preexisting inflammation associated with the subject's chronic hand eczema.**

[h] Photography will be performed at selected investigational sites. Photography will be optional. All efforts will be made to de-identify the subjects. Sites participating in optional photography will obtain photos of nail with the worst dystrophy at Baseline/Day 1 and at subsequent visits.

[i] A serum pregnancy test will be administered to all females of childbearing potential at Screening. A urine pregnancy test will be administered at Baseline, Weeks 4, 8, 12 and 13. A negative result is required for continued participation in the study, and results must be available prior to dispensing of investigational product.

[j] FSH will be performed (if indicated) at Screening to confirm post-menopausal status.

[k] PK assessments will be collected from all subjects at Days 1, 29 and 85. The draws will be pre-dose IP application in the clinic.

[l] Subjects to apply assigned IP in clinic at these visits. The time of application will be documented.

[m] Kits will be dispensed at Baseline, Weeks 2, 4 and 8. Dispensing at Week 12 requires approval from the Medical Monitor. See IP Handling Manual for details.

[n] Each IP tube will be weighed prior to dispensing at the Baseline visit and at each follow-up clinic visit according to the Schedule of Visits and Assessments. When IP is applied in the clinic, the IP tube will be weighed before and after IP application. See IP Handling Manual for details.

[o] Compliance calculation is described in the IP Handling Manual.

[p] Any emergent AEs will be followed in the clinic for up to one month at the Investigator's discretion until resolved or otherwise judged as clinically stable.

4. STATISTICAL ANALYSIS AND REPORTING

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will primarily use SAS (release 9.4 or higher). If the use of other software is warranted, the final statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, mean, standard deviation (SD), median, minimum, and maximum.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population for each treatment group, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (i.e., the same number of decimal places) as the observed data. Measures of location (mean and median) will be reported to 1 degree of precision more than the observed data and measures of spread (SD, standard error [SE]) will be reported to 2 degrees of precision more than the observed data.

Percentages will be presented to 1 decimal place, unless otherwise specified.

Unless otherwise indicated, all statistical tests will be conducted at the 0.1 significance level using 2-tailed tests, and *P* values will be reported. For the purposes of statistical comparisons, the vehicle BID and vehicle QD groups will be pooled together. Testing will be performed for:

- ARQ-252 cream 0.3% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% BID versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.1% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream (all strengths and dose frequencies) versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% (all dose frequencies) versus vehicle cream (all dose frequencies)

Corresponding 90% and 95% confidence intervals (CIs) will be presented for statistical tests. Testing will be performed for the primary endpoint of IGA clear or almost clear, for change from baseline in the HECSI score, and for the percent change from baseline in the HECSI score; however, *P* values will be provided for informational purposes for other endpoints as specified in Section 8. The primary statistical comparisons and evaluations of secondary endpoints will not be adjusted for multiplicity.

4.2. Interim Analysis and Data Monitoring

No interim efficacy analyses are planned.

5. ANALYSIS POPULATIONS

The following analysis populations are planned for this study:

- **Safety Population (SAF):** The Safety population will include all subjects who are enrolled (Cohort 1) or randomized (Cohort 2) and received at least 1 confirmed dose of investigational product (IP). This population will be used for all safety analyses and will be defined separately for each cohort.
- **All Treated Population (ALLTRT):** The All Treated population will include all subjects in the Safety population in Cohort 1. This population will be the primary analysis population for the analysis of Cohort 1 efficacy endpoints.
- **Intent-To-Treat Population (ITT):** The ITT population will include all subjects randomized to Cohort 2. This population will be the primary analysis population for the analysis of Cohort 2 efficacy endpoints.
- **Per Protocol Population (PP)**: The PP population will include all subjects in the Safety population in Cohort 2, who were at least 80% compliant with study medication application, and showed no important deviations from the study protocol that would affect the interpretation of efficacy. This population will be used as a sensitivity analysis of Cohort 2 primary and select secondary efficacy endpoints (i.e., IGA, WI-NRS, and HECSI analyses).
- **Pruritus Population (PRU4):** The PRU4 population is a subset of the All Treated population (Cohort 1) and ITT population (Cohort 2) and includes subjects with WI-NRS score ≥4 at baseline. This population will be used for the analysis of achievement of a 4-point reduction in WI-NRS score as compared to baseline for this subset of subjects.
- **Pain NRS Population (PNRS4):** The PNRS4 population is a subset of the All Treated population (Cohort 1) and ITT population (Cohort 2) and includes subjects with Pain NRS score ≥4 at baseline. This population will be used for the analysis of achievement of a 4-point reduction in Pain NRS score as compared to baseline for this subset of subjects.
- **Pain NRS Population (PNRS3):** The PNRS3 population is a subset of the All Treated population (Cohort 1) and ITT population (Cohort 2) and includes subjects with Pain NRS score ≥3 at baseline. This population will be used for the analysis of achievement of a 3-point reduction in Pain NRS score as compared to baseline for this subset of subjects.
- **Pain NRS Population (PNRS2):** The PNRS2 population is a subset of the All Treated population (Cohort 1) and ITT population (Cohort 2) and includes subjects with Pain NRS score ≥2 at baseline. This population will be used for the analysis of achievement of a 2-point reduction in Pain NRS score as compared to baseline for this subset of subjects.
- **Nail Dystrophy Population (ND):** The ND population is a subset of the ITT population and includes subjects with nail dystrophy at baseline. This population will be used for the analysis of nail dystrophy for this subset of subjects.

- **Pharmacokinetic Population (PK):** The PK population will include all subjects receiving the active drug with sufficient plasma concentrations of ARQ-252 to define a profile, as determined by the pharmacokineticist. This population will be used for analyses of PK parameters.

Assignment of subjects to populations will be confirmed at a blinded data review meeting to be held before the study database is locked.

6. GENERAL ISSUES FOR STATISTICAL ANALYSIS

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

For assessments where time was recorded (e.g., ECG), the last observation recorded before the first application of study drug will be used as the baseline observation for all calculations of change from baseline. For assessments where time was not recorded (excluding WI-NRS and Pain NRS), the last observation recorded on or before the day of first application of study drug will be used as the baseline observation for all calculations of change from baseline. For WI-NRS and Pain NRS, since diaries were completed daily at home from the Baseline/Day 1 visit until end of treatment, baseline is defined as the last observation recorded before the day of first application of study drug.

For assessments that are collected both before and after application of study drug at the Baseline/Day 1 visit, the last observation recorded before the first dose of study will be used as the baseline observation. For assessments collected only after application of study drug, no baseline will be defined (except for subject local tolerability; in this case, baseline is defined as the first non-missing observation recorded after the first application of study drug). If the tolerability assessments are not done as per protocol Section 5.1.7, those records will be excluded from the analysis.

6.1.2. Adjustments for Covariates

Covariates for this study include pooled site group (see Section 6.1.6) and IGA severity at baseline (mild, moderate, or severe). Subgroup analyses may be generated for the baseline covariates.

6.1.3. Multiple Comparisons

No adjustments for multiple comparisons will be made for this study.

6.1.4. Handling of Dropouts or Missing Data

Any subject who prematurely withdraws from the study will have their last available data assigned to an analysis window as described in Section 6.1.5.

For the primary efficacy endpoint of IGA score (Phase 2b/Cohort 2 only), the primary analysis will impute missing values using a regression-based multiple imputation model. This is a three step process.

1. The first step is to understand the pattern of missingness. In order to perform the multiple imputation, a monotone missing pattern has to be achieved. For example, if there exist values for baseline, Week 8, and Week 12 visits, but missing values for the Week 2 or 4 visits, the Markov-Chain Monte-Carlo (MCMC) method will be used to impute the small amount of missing data that may be missing at the intermediate visits that is required to make the missing data pattern monotone before applying the multiple imputation algorithm. This method uses a non-informative Jeffreys prior to derive the posterior mode from the expectation-maximization (EM) algorithm as the starting values for the MCMC method. MCMC method will use seed of 74746759. The IGA score will be treated as a continuous variable for this step. To avoid values that could not be observed in practice, imputed values will be constrained to be integers in the range of 0 to 4.
    a. The table below will determine the number of datasets to be imputed in this step. Determine the proportion of datapoints with non-monotone pattern across all visits and subjects which could be derived as a percentage of number of nonmonotone data points/total number of expected data points.

       This can be determined as $\frac{number\ of\ non\ montone\ visits}{total\ number\ of\ visits\ across\ all\ subjects} * 100$

Non-monotone Missing Data	Number of Imputed Datasets
≤ 2%	1
> 2% to ≤ 5%	3
> 5%	10

2. Once the monotone pattern is achieved, the next step is to implement the imputation algorithm. For this, the Predictive Mean Matching method (PMM) will be used. This method is particularly helpful if the normality assumption is violated. For subjects with complete data up to a particular visit, a PMM model will be fit that includes the outcome at that visit as the dependent variable and as independent variables, IGA score outcomes at previous visits, treatment group, and pooled site group using a seed of 88734121. This process will be repeated 25 times, resulting in a total of 25 to 250 complete analysis

datasets, depending on the number of imputed monotone datasets that are required. The seed or number of imputed datasets may be changed after unblinding in case of any issues with the imputation process, and it will be documented in the CSR if any change is required.

3. For each completed dataset, compute the necessary derived variables. The dichotomous success rate (clear or almost clear) will be derived. The results obtained will be analyzed using the CMH analysis for each of the complete analysis data sets stratified by baseline IGA score and site. The results will be combined into one multiple imputation inference (odds ratio, associated CI, and *P* value) using PROC MIANALYZE as illustrated below (Ratitch 2013).

This approach to imputation should be superior to other strategies such as carrying forward the last available observation, which may yield unrealistic imputed values. Also, the use of multiple imputation avoids the problem of artificially increasing power through data imputation associated with single-imputation methods because it accounts for the uncertainty associated with the imputation. Other missing data will not be imputed, with the exception of incomplete dates as described in Section 6.1.8. For responder analyses, missing data will be treated as a nonresponse with the exception of IGA. Only observed data will be summarized using descriptive statistics.

The SAS pseudo code for the multiple imputation process is listed below:

Step 1:

```
proc mi data=example seed=74746759 nimpute=XX round=1 out=example_1;
  mcmc impute=monotone;
  var <baseline score> …… <visit12 score>;
run;
```

Step 2:

```
proc mi data=example_1 seed=88734121 nimpute=XX  out=example_2;
  class <treatment> <site>;
  monotone regpmm(<baseline score> …… <visit12 score>);
  var <treatment> <site> <baseline score> …… <visit12 score>;
run;

XX will be the determined based on the proportion of missing data across visits.
```

Step 3: This step involves running CMH test stratified by baseline IGA score and site on each completed dataset and combining the results using PROC MIANALYZE.

```
proc freq data=example noprint;
  by <imputationnumber> <visit> ;
  tables <site> * <BL IGA> * <treatment> * <outcome> / cmh alpha=0.1;
  output out=example_stat cmh;
run;
```

In order to apply PROC MIANALYZE, normalizing transformations have to be applied to odds ratio. *P* values are obtained using Wilson Hilferty transformation as illustrated (Ratitch 2013).

6.1.5. Analysis Visit Windows

6.1.5.1. Non-Diary Assessments

Visits will be analyzed as scheduled (i.e., not subject to visit windowing). Unscheduled, early termination, and/or repeated measurements will only be included if a scheduled measurement is not available and the unscheduled, early termination, or repeated measurement falls within the analysis visit windows as described in Table 3 (Cohort 1 [Phase 1]) and Table 4 (Cohort 2 [Phase 2b]). The windows follow the Schedule of Events in Table 1 and Table 2. Visits falling outside of these windows will not be windowed (e.g., an unscheduled visit before first application of study drug). Unscheduled/repeated measurements will be listed.

Table 3: Analysis Visit Windows (Cohort 1 [Phase 1])

Visit Name	Analysis Visit Number	Target Start Day	Lower Limit	Upper Limit
Week 1	2	8	2	11
Week 2	3	15	12	18
Week 3	4	22	19	--

Table 4: Analysis Visit Windows (Cohort 2 [Phase 2b])

Visit Name	Analysis Visit Number	Target Start Day	Lower Limit	Upper Limit
Week 2	3	14	2	22
Week 4	5	28	23	42
Week 8	6	56	43	70
Week 12	7	85	71	90
Week 13	8	92	91	--

6.1.5.2. Diary Assessments (WI-NRS, Pain NRS)

Diary entries will be assigned to a study week for analysis based on the study day relative to the first application of study drug according to Table 5 (Cohort 1 [Phase 1]) and Table 6 (Cohort 2 [Phase 2]).

Table 5: Analysis Visit Windows (Cohort 1 [Phase 1])

Visit Name	Analysis Visit Number	Lower Limit	Upper Limit
Study Week 1	101	1	7
Study Week 2	102	8	14 [#]

[#] Data may have been collected for subjects past Day 14; any Diary entries recorded after this day will not be presented in any summaries. However, all Diary entries will be presented in the data listings; entries after Day 14 will be presented as Week >2.

Table 6: Analysis Visit Windows (Cohort 2 [Phase 2b])

Visit Name	Analysis Visit Number	Lower Limit	Upper Limit
Study Week 1	101	1	7
Study Week 2	102	8	14
Study Week 3	103	15	21
Study Week 4	104	22	28
Study Week 5	105	29	35
Study Week 6	106	36	42
Study Week 7	107	43	49
Study Week 8	108	50	56
Study Week 9	109	57	63
Study Week 10	110	64	70
Study Week 11	111	71	77
Study Week 12	112	78	84
Study Week 13	113	85	91 [#]

[#] Data may have been collected for subjects past Day 91; any Diary entries recorded after this day will not be presented in any summaries. However, all Diary entries will be presented in the data listings; entries after Day 91 will be presented as Week >13.

6.1.6. Pooling of Sites

Sites will be pooled for statistical analysis as follows. For analysis, sites should have a minimum of 10 randomized subjects. The smallest sites will be grouped sequentially in order of smallest to largest within each country, restricting to those sites that did not meet the minimum enrollment of 10, until each pooled site has a minimum of 10 subjects within each country with at least 1 subject in each treatment group.

6.1.7. Derived Variables

- **Study Week =** 7-day periods starting on Day 1, as described in Section 6.1.5.2. For example, Study Week 1 corresponds to Days 1 to 7. This is in contrast to **Study Visit**, which describes the actual clinic visit week. The nomenclature of "Study Week" will be used with respect Pain NRS and WI-NRS analyses; otherwise, "Study Visit" will be used.
- **IGA Improvement =** achievement of at least a 2-point improvement (i.e., reduction) in IGA score from baseline.
- **IGA Success =** post-baseline IGA of "Clear" or "Almost Clear" PLUS achievement of at least a 2-point improvement (i.e., reduction) in IGA score from baseline.
- **Average Weekly WI-NRS Pruritus Score** = WI-NRS pruritus scores will be assigned to a particular study week based on the study week window, as shown in Section 6.1.5.2. If 2 or more observations are present for a single day, those observations will be averaged into a single daily value before calculating the average weekly score. The average of the reported (non-missing) WI-NRS pruritus scores assigned to each study week will be calculated. If at least 1 WI-NRS pruritus score is present in this time period, the average weekly WI-NRS pruritus score will be calculated; otherwise the average weekly score will be missing for that week.
- **WI-NRS 4-point Reduction** = achievement of a 4-point reduction in WI-NRS pruritus score at each study week compared to baseline, calculated only for subjects with a WI-NRS pruritus score of ≥ 4 at baseline (PRU4 population).
- **HECSI Fingertips Subscore** = (E + I + V + F + S + O) * Ex,

  where E, I, V, F, S, and O, are erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe); Ex is estimated area of skin involved, graded on a scale of 0 to 4. The range for the HECSI Fingertips subscore is 0 to 72. If any of the component scores are missing, the HECSI Fingertips subscore cannot be calculated; however, if the estimated area of skin involved = 0, the HECSI Fingertips subscore will be set to 0. Lower scores indicate better outcomes.
- **HECSI Fingers (except tips) Subscore** = (E + I + V + F + S + O) * Ex,

  where E, I, V, F, S, and O, are erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe); Ex is estimated area of skin involved, graded on a scale of 0 to 4. The range for the HECSI Fingers (except tips) subscore is 0 to 72. If any of the component scores are missing, the HECSI Fingers (except tips) subscore cannot be calculated; however, if the estimated area of skin

involved = 0, the HECSI Fingers (except tips) subscore will be set to 0. Lower scores indicate better outcomes.

- **HECSI Palm of Hands Subscore** = (E + I + V + F + S + O) * Ex,

  where E, I, V, F, S, and O, are erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe); Ex is estimated area of skin involved, graded on a scale of 0 to 4. The range for the HECSI Palm of Hands subscore is 0 to 72. If any of the component scores are missing, the HECSI Palm of Hands subscore cannot be calculated; however, if the estimated area of skin involved = 0, the HECSI Palm of Hands subscore will be set to 0. Lower scores indicate better outcomes.
- **HECSI Back of Hands Subscore** = (E + I + V + F + S + O) * Ex,

  where E, I, V, F, S, and O, are erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe); Ex is estimated area of skin involved, graded on a scale of 0 to 4. The range for the HECSI Back of Hands subscore is 0 to 72. If any of the component scores are missing, the HECSI Back of Hands subscore cannot be calculated; however, if the estimated area of skin involved = 0, the HECSI Back of Hands subscore will be set to 0. Lower scores indicate better outcomes.
- **HECSI Wrists Subscore** = (E + I + V + F + S + O) * Ex,

  where E, I, V, F, S, and O, are erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe); Ex is estimated area of skin involved, graded on a scale of 0 to 4. The range for the HECSI Wrists subscore is 0 to 72. If any of the component scores are missing, the HECSI Wrists subscore cannot be calculated; however, if the estimated area of skin involved = 0, the HECSI Wrists subscore will be set to 0. Lower scores indicate better outcomes.
- **HECSI Total Score** = sum of HECSI Fingertips, Fingers (except tips), Palm of Hands, Back of Hands, and Wrists subscores. The range for the HECSI Total score is 0 to 360. Lower scores indicate better outcomes.
- **HECSI-75 =** achievement of a 75% reduction in HECSI total score from baseline.
- **Average Weekly Pain NRS Score** = Pain NRS scores will be assigned to a particular study week based on the study week window, as shown in Section 6.1.5.2. If 2 or more observations are present for a single day, those observations will be averaged into a single daily value before calculating the average weekly score. The average of the reported (non-missing) Pain NRS scores assigned to each study week will be calculated. If at least 1 Pain NRS score is present in this time period, the average weekly Pain NRS score will be calculated; otherwise the average weekly score will be missing for that week.
- **Pain NRS 4-point Reduction** = achievement of a 4-point reduction in Pain NRS score at each study week compared to baseline, calculated only for subjects with a Pain NRS score of ≥ 4 at baseline (PNRS4 population).

- **QOLHEQ Symptoms Subscore =** sum of QOLHEQ questions 1, 6, 9, 11, 20, 23, and 28. Questions 1, 6, 9, 11, 20, and 23 are scored such that never = 0, rarely = 1, sometimes = 2, often = 3, and all the time = 4; question 28 is scored such that never = 0, rarely = 1, sometimes = 1, often = 2, and all the time = 3. The range for QOLHEQ Symptoms subscore is 0 to 27, where lower scores indicate better outcomes. If 1 question has a missing result, set the missing result to 0 before summing; if more than 1 question is missing, then the QOLHEQ Symptoms subscore cannot be calculated.
- **QOLHEQ Emotions Subscore =** sum of QOLHEQ questions 5, 8, 10, 16, 19, 21, 27, and 30. Questions 5, 8, 16, 19, 21, 27, and 30 are scored such that never = 0, rarely = 1, sometimes = 2, often = 3, and all the time = 4; question 10 is scored such that never = 0, rarely = 1, sometimes = 1, often = 2, and all the time = 3. The range for QOLHEQ Emotions subscore is 0 to 31, where lower scores indicate better outcomes. If 1 question has a missing result, set the missing result to 0 before summing; if more than 1 question is missing, then the QOLHEQ Emotions subscore cannot be calculated.
- **QOLHEQ Limitations in Functioning Subscore =** sum of QOLHEQ questions 2, 3, 12, 14, 15, 17, 25, and 29. All questions are scored such that never = 0, rarely = 1, sometimes = 2, often = 3, and all the time = 4. The range for QOLHEQ Limitations in Functioning subscore is 0 to 32, where lower scores indicate better outcomes. If 1 question has a missing result, set the missing result to 0 before summing; if more than 1 question is missing, then the QOLHEQ Limitations in Functioning subscore cannot be calculated.
- **QOLHEQ Treatment and Prevention Subscore =** sum of QOLHEQ questions 4, 7, 13, 18, 22, 24, and 26. Questions 7, 13, 18, 22, 24, and 26 are scored such that never = 0, rarely = 1, sometimes = 2, often = 3, and all the time = 4; question 4 is scored such that never = 0, rarely = 1, sometimes = 1, often = 2, and all the time = 3. The range for QOLHEQ Treatment and Prevention subscore is 0 to 27, where lower scores indicate better outcomes. If 1 question has a missing result, set the missing result to 0 before summing; if more than 1 question is missing, then the QOLHEQ Treatment and Prevention subscore cannot be calculated.
- **QOLHEQ Total Score =** sum of all 30 QOLHEQ questions. Questions 4, 10, and 28 are scored such that never = 0, rarely = 1, sometimes = 1, often = 2, and all the time = 3; otherwise, questions are scored such that never = 0, rarely = 1, sometimes = 2, often = 3, and all the time = 4. The range for QOLHEQ Total score is 0 to 117, where lower scores indicate better outcomes. If 1 to 3 questions have a missing result, set the missing result to 0 before summing; if more than 3 questions are missing, then the QOLHEQ Total score cannot be calculated.
- **Total Hand % BSA Affected by Disease =** sum of % BSA affected by disease from the following hand areas: left palmar, left dorsal, right palmar, and right dorsal. All 4 hand areas must have a result for the total hand % BSA affected by disease to be calculated.
- **Compliance** = number of applications divided by the expected number of investigational product (IP) applications for each subject. Compliance will be calculated using drug accountability data over the entire treatment period for each subject, up to treatment completion or discontinuation.

- **Number of Expected IP Applications (BID dosing)** = 170 (Cohort 2 BID) for subjects who complete the study or number of days between first and last application of IP, derived as 2 * (last treatment date - first treatment date + 1), for subjects who discontinue early from the study.
- **Number of Expected IP Applications (QD dosing)** = 30 (Cohort 1) or 85 (Cohort 2 QD) for subjects who complete the study or number of days between first and last application of IP, derived as (last treatment date - first treatment date + 1), for subjects who discontinue early from the study.
- **Number of IP Applications =** number of expected IP applications – missed IP applications as collected in the electronic case report form (eCRF).

- **Weight of IP (g)** = returned tube weight – dispensed tube weight.
- **Body Mass Index (BMI) (kg/m^2)** = [weight (kg) / height (cm) / height (cm)] x 10,000.
- **Change from Baseline** = value at current time point – value at baseline.
- **Treatment Emergent AE (TEAE)** = any AE with an onset date/time after the first application of IP. If time is unavailable, any AE occurring on or after the date of first application of IP will be considered treatment emergent.
- **Completion of Study =** Completion of the primary efficacy assessment (IGA) at Week 12. This may differ than what was recorded in the eCRF.

6.1.8. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

All *P* values will be displayed in four decimals and rounded using standard scientific notation (e.g., 0.XXXX). If a *P* value less than 0.0001 occurs it will be shown in tables as <0.0001; similarly, if a *P* value greater than 0.9999 occurs it will be shown in tables as >0.9999.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0 thesaurus.

Medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO-DDE) Global B3 version September 2019.

A treatment-related AE is any AE with a relationship to the study drug of possibly related, probably related, likely related, or missing.

For partial AE and medication start dates:

- If the year is unknown, then do not impute the date but assign a missing value.
- If the year is known, but the month or month and day is unknown, then:
  - If the year matches the year of first dose date and the end date (if present) is after first dose date, then impute as the month and day of the first dose date.
  - Otherwise, assign 01 January.

- If the year and month are known, but the day is unknown, then:
  - If the month and year match the month and year of the first dose date, then impute as the day of the first dose date.
  - Otherwise, assign 01.

For partial AE and medication end dates:

- If the year is unknown, then do not impute the date but assign as missing value.
- If the year is known, but the month or month and day is unknown, then:
  - If the year matches the year of the last date of the study (date of last contact if subject lost to follow-up; date of completion or early termination otherwise), then impute as the month and day of the last date of the study.
  - Otherwise, assign 31 December.
- If the year and month are known, but the day is unknown, then:
  - If the month and year match the month and year of the last date of the study, then impute as the day of the last date of the study.
  - Otherwise, assign the last day of the month.

These conventions will be applied to AE and medication onset dates and times with the following precaution: if the missing date and time reflect the date and time of onset of an AE, the modified date and time will be constructed to match the first documented date/time post drug administration while preserving the order in which the AE was reported in the eCRF.

In cases where variables for questionnaires were derived in the eCRF (e.g., total scores) and a derivation is indicated in Section 6.1.7, the results as derived by statistics (as opposed to the results derived in the eCRF) will be used in analysis.

6.1.9. Presentation of Cohorts and Treatments in Summaries

Study subjects and demographic summaries will be presented by cohort and treatment in the same output, as follows:

- Cohorts 1 and 2: Cohort 1 (ARQ-252 cream 0.3% QD); Cohort 2 (ARQ-252 cream 0.3% QD, ARQ-252 cream 0.3% BID, ARQ-252 cream 0.1% BID, vehicle cream QD, and vehicle cream BID)

Efficacy data will be presented separately for each cohort (where the efficacy parameter was collected for subjects in Cohort 1), as follows:

- Cohort 1: ARQ-252 cream 0.3% QD
- Cohort 2: ARQ-252 cream 0.3% QD, ARQ-252 cream 0.3% BID, ARQ-252 cream 0.1% BID, and vehicle cream (all dose frequencies)
- Cohort 2, Pooled Treatments: ARQ-252 cream (all strengths/dose frequencies), ARQ-252 cream 0.3% (all dose frequencies), and vehicle cream (all dose frequencies)

Safety summaries will be presented by cohort and treatment in the same output where possible, as follows:

- Cohorts 1 and 2: Cohort 1 (ARQ-252 cream 0.3% QD); Cohort 2 (ARQ-252 cream 0.3% QD, ARQ-252 cream 0.3% BID, ARQ-252 cream 0.1% BID, vehicle cream QD, and vehicle cream BID)

Otherwise, safety summaries will be presented separately for each cohort, as follows:

- Cohort 1: ARQ-252 cream 0.3% QD
- Cohort 2: ARQ-252 cream 0.3% QD, ARQ-252 cream 0.3% BID, ARQ-252 cream 0.1% BID, vehicle cream QD, and vehicle cream BID

6.2. Special Handling for COVID-19 Disruptions

In some cases, study visits will have to be delayed/not performed as a result of COVID-19 disruptions (e.g., sites were closed or subjects were under stay-at-home orders). Where possible, study sites may collect post-baseline data from subjects remotely by telephone, traditional mail, and/or email; this will be clearly documented in the source. If possible, sites should adhere to the protocol visit window for remote data collection.

Investigator assessments and subject questionnaires normally completed during on-site visits should be completed on the appropriate paper source documents. The following assessments/questionnaires are approved to be collected via telemedicine/remotely:

- WI-NRS
- Pain NRS
- Subject Local Tolerability
- QOLHEQ
- IP / diary compliance

The following assessments cannot be completed via telemedicine/remotely:

- IGA
- BSA
- Investigator Local Tolerability
- Subject Weight
- HECSI
- Nail Dystrophy Assessment

Study visits and procedures must be followed per protocol whenever possible. Any specific changes in study conduct that deviate from the protocol should be communicated to the institutional review board and Sponsor. All protocol deviations which occurred as a result of COVID-19 disruptions (e.g., visits out of window, missed assessments, etc.) will be differentiated from other protocol deviations.

7. STUDY SUBJECTS AND DEMOGRAPHICS

Presentation of treatments for the study subjects and demographics summary tables are described in Section 6.1.9.

7.1. Disposition of Subjects and Withdrawals

Disposition will include tabulations of the number of subjects enrolled (Cohort 1) or randomized into each treatment group (Cohort 2), the number of subjects who received treatment, subjects completing the study, tabulated reasons for discontinuation from the study, including whether or not the subject did not complete the study due to COVID-19 disruption and reasons, and number of subjects in each analysis population. Disposition will be summarized for all subjects who were entered into the database by treatment group within cohort. This summary will be based on all enrolled (Cohort 1) or randomized (Cohort 2) subjects.

7.2. Protocol Violations and Deviations

The number of subjects with important protocol deviations and/or eligibility deviations will be summarized in categories by treatment group within cohort for subjects in Safety population; the incidence of all protocol deviations will also be provided. All protocol deviations will be provided in the data listings.

7.3. Demographics and Other Baseline Characteristics

Summary statistics for age, gender (including child-bearing potential), race, ethnicity, height, weight, percent BSA affected by disease (dorsal [left hand], dorsal [right hand], palmar [left hand], palmar [right hand], total hand), BMI, and baseline disease characteristics (IGA, WI-NRS, HECSI subscores and total score, Pain NRS, and QOLHEQ subscores and total score) will be presented by treatment group within cohort, as well as for overall subjects across both cohorts.

A summary of chronic hand eczema history, including primary morphologic subtype of hand eczema, patch test results, and distribution of chronic hand eczema (presence of eczema on each hand on the following surfaces: palmar [including lateral aspects of fingers], dorsal, interdigital, and pulpitis) will be presented by treatment group within cohort.

The number and percent of subjects reporting various medical histories, grouped by MedDRA system organ class and preferred term, will be tabulated by treatment group within cohort.

For the continuous variables, the number of nonmissing values and the mean, SD, minimum, median and maximum will be tabulated.

For ordinal variables such as the IGA, WI-NRS, and Pain NRS, summary statistics including the mean, median, and range of the ordinal variable will be presented, as well as frequency counts of each level of the ordinal variable.

For the categorical variables, the counts and proportions of each value will be tabulated.

These analyses will be conducted for the ITT and Safety populations, except for chronic hand eczema history summary, which will only be summarized on the Safety population.

7.4. Exposure and Compliance

The number of IP applications by each subject based on diary data will be summarized using descriptive statistics appropriate for continuous variables.

The amount of IP each subject used based on tube weight will be summarized descriptively by treatment group using continuous methods.

A subject will be considered compliant with the dosing regimen if the subject applies at least 80% of the expected applications during the IP application period and does not miss more than 3 consecutive days of dosing.

Investigational product application compliance will be calculated based on number of applications divided by the expected number of IP applications. Compliance will be summarized descriptively by treatment group using the following categories:

>100%
≥80% - ≤100%
<80%

8. EFFICACY ANALYSIS

The statistical models described in this section apply to subjects in Cohort 2 (Phase 2b) only, unless otherwise specified. Presentation of treatments for the efficacy summary tables are described in Section 6.1.9.

8.1. Primary Efficacy Analysis

8.1.1. Investigator Global Assessment (IGA) Score of "Clear" or "Almost Clear" at Week 12

The IGA is a static evaluation of qualitative overall chronic hand eczema severity. This global assessment scale is an ordinal scale with five severity grades (reported only in integers of 0 to 4). Each IGA Severity Score is defined by distinct and clinically relevant morphologic descriptions that minimizes inter-observer variability. Table 7 illustrates the description of each severity grade.

Table 7: IGA

Score	Grade	Description
0	Clear	Absence of erythema and scaling, **AND**
		Absence of vesiculation, edema, and fissures. Note: Post-inflammatory pigmentary changes may be present.
1	Almost clear	Barely perceptible or faint erythema, **and/or** Slight flaking over limited areas, mostly fine scales, **AND**
		Absence of vesiculation, edema, or fissures
2	Mild	Barely perceptible or faint erythema, **and/or** Slight flaking over limited areas, mostly fine scales **AND**
		Scattered vesicles affecting up to 10% of hand, without erosion, **and/or** Dermal swelling over less than 10% of hands, **and/or** Cracked skin affecting a small area of the hand
3	Moderate	Either barely perceptible or faint erythema, or prominent redness, **and/or** Either slight flaking over limited areas, mostly fine scales, or flaking over widespread area(s), coarser scale **AND**
		Scattered or clustered vesicles affecting up to 30% of hand, without visible erosion or excoriation, **and/or** Definite dermal swelling over more than 10% of hand, **and/or** Cracked skin affecting multiple areas of the hand
4	Severe	Either prominent or deep intense red color, **and/or** Either flaking over widespread area(s), coarser scales, or desquamation covering over 30% of the hand, with coarse thick scales **AND**
		At least one of the following: High density of vesicles extending over large area(s), or with erosion or excoriation, **and/or** Dermal swelling with skin induration over widespread area(s), **and/or** One or more deep fissures and causing bleeding

Categorical Data Analysis

The primary efficacy endpoint is the rate of subjects achieving an IGA score of "Clear" or "Almost Clear" at Week 12.

The primary statistical comparisons for Cohort 2 subjects will be as follows:

- ARQ-252 cream 0.3% BID versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.1% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream (all strengths and dose frequencies) versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% (all dose frequencies) versus vehicle cream (all dose frequencies)

The primary endpoint will be analyzed using a CMH test stratified by pooled study site group and baseline IGA category. Statistical significance will be concluded at the 10% significance level (2-sided) or less, as discussed in Section 4.1. Odds ratios and 90% and 95% CIs for the odds ratios will be provided. Additionally, the 90% and 95% Wilson CIs for proportion of successes in each treatment group will be presented.

For the primary analysis, missing IGA scores will be imputed using multiple imputation as described in Section 6.1.4. These imputations will result in a minimum of 25 to a maximum of 250 complete analysis datasets, depending on the number of imputed monotone datasets required. The CMH analyses will be performed separately for each of the complete analysis data sets, and the results will be combined into one multiple imputation inference (estimated treatment effect and associated CI and *P* value).

The primary efficacy analysis will be based on Cohort 2 subjects in the ITT population.

8.1.2. Sensitivity Analyses of the Primary Efficacy Endpoint

The following sensitivity analyses will be performed, based on the CMH test as described in Section 8.1:

- The primary efficacy endpoint analysis, repeated on Cohort 2 subjects in the ITT and PP populations on nonimputed data; and
- The primary efficacy endpoint analysis (excluding the CMH testing), repeated on Cohort 1 subjects in the All Treated population on nonimputed data only.

8.2. Secondary Efficacy Analysis

All secondary efficacy analyses will be performed using the All Treated population for subjects in Cohort 1 and the ITT population for subjects in Cohort 2, unless otherwise specified.

The statistical comparisons for all secondary efficacy endpoints for Cohort 2 subjects will be as follows:

- ARQ-252 cream 0.3% BID versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.1% QD versus vehicle cream (all dose frequencies)
- ARQ-252 cream (all strengths and dose frequencies) versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% (all dose frequencies) versus vehicle cream (all dose frequencies)

8.2.1. Investigator Global Assessment (IGA)

Secondary efficacy endpoints relating to the IGA include the following:

- The rate of achievement of IGA of "clear" or "almost clear" PLUS at least a 2-point improvement from Baseline at Weeks 2, 4, 8, 12, and 13
- The rate of achievement of at least a 2-point improvement from baseline at Weeks 2, 4, 8, 12, and 13
- The rate of achievement of IGA of "clear" or "almost clear" at Weeks 2, 4, 8, and 13
- Change in IGA score at Weeks 2, 4, 8, 12, and 13 as compared to baseline

Rate of Achievement Analyses

Rate of achievement analyses will be performed using the same CMH test as described in Section 8.1 as follows:

- The rate of achievement of IGA of "clear" or "almost clear" PLUS at least a 2-point improvement from baseline will be analyzed on Cohort 2 subjects in the ITT population (imputed and nonimputed data) and PP population (nonimputed data only);
- The rate of achievement of at least a 2-point improvement from baseline will be analyzed on Cohort 2 subjects in the ITT population (imputed and nonimputed data); and
- The rate of achievement of IGA of "clear" or "almost clear" will be analyzed on Cohort 2 subjects in the ITT population (imputed and nonimputed data) and PP population (nonimputed data only).

Rate of achievement of IGA success (IGA score of "clear" or "almost clear" plus at least a 2-point improvement from baseline) will also be analyzed by baseline IGA score, for Cohort 2 subjects in the ITT population (imputed and nonimputed data). The proportion of subjects achieving IGA success at Week 12 will be presented by study site for Cohort 2 subjects in the ITT population (nonimputed data only). Additionally, a summary will be provided for subjects in

Cohort 1 in the All Treated population (nonimputed data only), however, this will not include the CMH test.

Change in IGA Score Analysis

Change and percent change from baseline to Weeks 2, 4, 8, 12, and 13 in IGA score will be analyzed using descriptive summaries and an analysis of covariance (ANCOVA) with terms for treatment group, pooled site group, and baseline IGA category as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The least-squares (LS) means, standard errors, 90% and 95% CIs, and *P* values will be presented. These summaries will be provided for Cohort 2 subjects in the ITT population (imputed and nonimputed data) and PP population (ANCOVA using nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding between-treatment contrasts (due to being a single-treatment cohort).

8.2.2. Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score

Secondary efficacy endpoints relating to WI-NRS pruritus score include the following:

- Change and percent change in WI-NRS pruritus score at Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 as compared to Baseline
- The rate of achievement of ≥4-point reduction from Baseline in WI-NRS pruritus score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first study drug application, in subjects with Baseline WI-NRS pruritus score of at least 4

Change in WI-NRS Pruritus Score Analysis

Change and percent change from baseline to each study week through Week 12 in average weekly WI-NRS pruritus score will be analyzed using descriptive statistics and an ANCOVA with terms for treatment group, pooled site group, baseline IGA category, and baseline WI-NRS pruritus score as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The LS means, standard errors, 90% and 95% CIs, and *P* values will be presented. This analysis will be based on Cohort 2 subjects in the ITT and PP populations (ANCOVA using nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding between-treatment contrasts (due to being a single-treatment cohort).

Rate of Achievement Analysis

In subjects with a baseline WI-NRS score ≥4, achievement of a ≥4-point improvement from baseline in average weekly WI-NRS score at Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 will be analyzed using CMH tests stratified by pooled site group and baseline IGA category similar to the primary analysis in Section 8.1, with the exception that missing data will not be replaced. Odds ratios and 90% and 95% CIs of the odds ratios will be provided. Additionally, the 90% and 95% Wilson CIs for proportion of successes in each treatment group will be presented. This analysis will be based on Cohort 2 subjects in the PRU4 population (nonimputed data only).

Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding the CMH test (due to being a single-treatment cohort).

8.2.3. Hand Eczema Severity Index (HECSI)

The secondary efficacy endpoints relating to HECSI are:

- Change and percent change in HECSI score at Weeks 2, 4, 8, 12, and 13 compared to Baseline
- Achievement of HECSI-75

The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). Derivations for each of the subscores and the total score can be found in Section 6.1.7.

Change and percent change from baseline to Weeks 2, 4, 8, 12, and 13 in HECSI subscores (Fingertips, Fingers [except Tips], Palm of Hands, Back of Hands, and Wrists) and total score will be analyzed using descriptive statistics and an ANCOVA with terms for treatment group, pooled site group, baseline IGA category, and baseline HECSI score as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The LS means, standard errors, 90% and 95% CIs, and *P* values will be presented. This analysis will be based on Cohort 2 subjects in the ITT population (nonimputed data only) and PP population (ANCOVA using nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding between-treatment contrasts (due to being a single-treatment cohort).

Frequencies and percentages of subjects achieving HECSI-75 will be presented by study vist and treatment group. This endpoint will be analyzed using CMH tests stratified by pooled site group and baseline IGA category similar to the primary analysis in Section 8.1, with the exception that missing data will not be replaced. Odds ratios and 90% and 95% CIs of the odds ratios will be provided. Additionally, the 90% and 95% Wilson CIs for proportion of subjects achieving 75% reduction in each treatment group will be presented. This analysis will be based on Cohort 2 subjects in the ITT and PP populations (nonimputed data only).

8.2.4. Pain Numeric Rating Scale (NRS) Score

Secondary efficacy endpoints relating to Pain NRS score include the following:

- Change and percent change in Pain NRS score from Baseline to Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13
- The rate of achievement of ≥4-point reduction from Baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug with Baseline Pain NRS score of at least 4

- The rate of achievement of ≥3-point reduction from Baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 3
- The rate of achievement of ≥2-point reduction from Baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 2

The Pain NRS score is the subject's assessment of worst pain intensity over the past 24 hours on a scale of 0 to 10, where 0 = "no pain" and 10 = "worst possible pain".

Change in Pain NRS Score Analysis

Change and percent from baseline to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in average weekly Pain NRS score will be analyzed using descriptive statistics and an ANCOVA with terms for treatment group, pooled site group, baseline IGA category, and baseline Pain NRS score as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The LS means, standard errors, 90% and 95% CIs, and *P* values will be presented. This analysis will be based on Cohort 2 subjects in the ITT population (nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding between-treatment contrasts (due to being a single-treatment cohort).

Rate of Achievement Analysis

In subjects with a baseline Pain NRS score ≥4, achievement of a ≥4-point improvement from baseline in average weekly Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug will be analyzed using CMH tests stratified by pooled site group and baseline IGA category similar to the primary analysis in Section 8.1, with the exception that missing data will not be replaced. Odds ratios and 90% and 95% CIs of the odds ratios will be provided. Additionally, the 90% and 95% Wilson CIs for proportion of successes in each treatment group will be presented. This analysis will be based on Cohort 2 subjects in the PNRS4 population (nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the PNRS4 population, excluding the CMH test (due to being a single-treatment cohort).

This analysis will furthermore be repeated on subjects with a baseline Pain NRS score ≥3 and a baseline Pain NRS score ≥2 for achievement of a ≥3-point improvement from baseline and a ≥2-point improvement from baseline, respectively. This analysis will be performed on subjects in the PNRS3 and PNRS2 populations, with each cohort presented separately (where the CMH testing in Cohort 1 will be excluded).

8.2.5. Quality of Life in Hand Eczema Questionnaire (QOLHEQ)

The secondary efficacy endpoint relating to QOLHEQ is:

- Change and percent change from baseline in overall QOLHEQ score at each study visit

The construct HRQOL includes all impairments or limiting conditions caused by the health state of an individual. The QOLHEQ is a disease specific instrument, thereby only assessing impairments caused by hand eczema. It consists of 30 items which can be summarized according to four domains of HRQOL: Impairments because of (1) symptoms, (2) emotions, (3) limitations in functioning, or (4) because of treatment and prevention. Derivations for each of the subscores and the total score can be found in Section 6.1.7.

Change and percent change from baseline to Weeks 2, 4, 8, 12, and 13 in QOLHEQ subscores (Symptoms, Emotions, Limitations in Function, Treatment and Prevention) and total score will be analyzed using descriptive statistics and an ANCOVA with terms for treatment group, pooled site group, baseline IGA category, and baseline overall QOLHEQ score as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The LS means, standard errors, 90% and 95% CIs, and *P* values will be presented. These analyses will be based on Cohort 2 subjects in the ITT population (nonimputed data only).

8.2.6. Percent Body Surface Area (BSA) Affected by Disease

The secondary efficacy endpoint relating to percent BSA affected by disease (dorsal [left hand], dorsal [right hand], palmar [left hand], palmar [right hand], total hand) is:

- Percent BSA affected by disease and % change from baseline in BSA affected by disease at baseline, 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 13 weeks

Change and percent change from baseline to Weeks 2, 4, 8, 12, and 13 in percent BSA affected by disease will be analyzed using descriptive statistics and an ANCOVA with terms for treatment group, pooled site group, baseline IGA category, and baseline percent BSA affected by disease as covariates, by study visit. Statistical comparisons between the treatment groups will be obtained using contrasts. The LS means, standard errors, 90% and 95% CIs, and *P* values will be presented. This analysis will be based on Cohort 2 subjects in the ITT population (nonimputed data only). Additionally, this analysis will be repeated for Cohort 1 subjects in the All Treated population, excluding between-treatment contrasts (due to being a single-treatment cohort).

8.3. Exploratory Efficacy Analysis

The exploratory efficacy endpoint is:

- Change from Baseline in Nail Dystrophy at each visit

In subjects with a nail dystrophy at baseline, change in number of millimeters of normal-appearing nail distal to the cuticle will be summarized by treatment group and study visit. Since the number if millimeters of normal-appearing nail distal to the cuticle at baseline was not collected, it is assumed to be 0 mm; similarly, for subjects with nail dystrophy at baseline, if they report having no normal-appearing nail distal to the cuticle after baseline, their result is imputed as 0 mm (as this amount is not collected in the eCRF). This analysis will be based on Cohort 2 subjects in the ND population (nonimputed data only).

9. SAFETY AND TOLERABILITY ANALYSIS

Safety will be evaluated from reported AEs, physical examinations, local tolerability assessments, changes in clinical laboratory values, and changes in vital signs/weight. No inferential statistical tests will be performed.

All safety analyses will be performed on the Safety population.

Presentation of treatments for safety analysis summary tables are described in Section 6.1.9.

9.1. Adverse Events

All AEs, TEAEs, and SAEs will be coded using the MedDRA dictionary version 23.0.

A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. An overall summary of TEAEs will be provided; this will present number and percent of subjects who reported at least 1 of the following: TEAE (including all TEAEs, TEAEs by maximum severity, and related TEAEs), SAE, discontinued the study due to a TEAE, discontinued the study drug due to a TEAE, or a TEAE resulting in death.

The number and percent of subjects reporting TEAEs, grouped by MedDRA system organ class (SOC) and preferred term, will be tabulated by severity or by greatest relationship to study drug and treatment group within cohort. In the case of multiple occurrences of the same TEAE within the same subject, each subject will only be counted once for each preferred term. Additionally, the number and percent of subjects reporting related TEAEs will be summarized by MedDRA SOC, preferred term, severity, and treatment group within cohort.

Relationship to study drug will be mapped as follows: related = likely related, probably related, or possibly related; unrelated = unlikely related or unrelated. In the summaries showing severity and relationship to study medication the event with the maximum severity (mild < moderate < severe < life-threatening < death) or strongest relationship (unrelated < related) will be reported. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = severe, relationship = related).

In the AE data listings, all AEs will be displayed. Any AEs that are treatment emergent will be flagged.

9.1.1. Adverse Events Leading to Withdrawal

A summary of incidence rates (frequencies and percentages) of TEAEs leading to withdrawal of study drug by treatment group within cohort, SOC, and preferred term will be prepared for the Safety population. Additionally, this table will be repeated for related TEAEs leading to withdrawal of study drug and all TEAEs leading to withdrawal from the study. No inferential statistical tests will be performed.

A data listing of AEs leading to withdrawal of study drug will also be provided, displaying details of the event(s) captured on the eCRF.

9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study will be listed.

Serious adverse events (SAEs) will be listed and tabulated by SOC and preferred term and presented by treatment group within cohort, by severity, and by relationship to study treatment.

9.2. Local Tolerability Assessments

The investigator's assessment of the application site reaction will be summarized by study visit and treatment group within cohort using both categorical methods (number and percentage of subjects with each score) as well as continuous methods (e.g., mean, median). Categorical summaries will be provided for dermal response as well as other effects. No inferential statistical tests will be performed.

The subject's assessment of the application site reaction will be summarized similarly.

9.3. Clinical Laboratory Evaluations

Laboratory test results will be summarized descriptively by treatment and study visit as both observed values and change from baseline values for continuous hematology, chemistry (including thyroid), and urinalysis results. Categorical urinalysis results will be summarized using frequencies by study visit and treatment group within cohort.

The number of subjects with clinical laboratory values below, within, or above the normal range by study visit and in relation to baseline will be tabulated for each clinical laboratory analyte by treatment group within cohort (shift table).

Abnormal results will be flagged in the listings. In addition, pregnancy test results and hormonal laboratory results will be listed.

9.4. Vital Signs

Descriptive summaries of observed values and changes from baseline will be calculated for systolic blood pressure, diastolic blood pressure, heart rate, height, weight, BMI, and oral body temperature by treatment group within cohort and study visit.

9.5. 12-Lead Electrocardiograms

Descriptive summaries for observed values and change from baseline will be presented for 12-lead electrocardiogram (ECG) measures of PR interval, QRS interval, QT interval, QTc interval (Fridericia's [QTcF] correction method), and heart rate. These summaries will be presented by study visit and treatment group within cohort.

The number and percentage of subjects with each ECG investigator interpretation (normal; abnormal, not clinically significant; or abnormal, clinically significant) will be displayed for each treatment group within cohort and study visit.

9.6. Physical Examination

The number and percentage of subjects with normal and abnormal findings in the physical examination will be displayed at each study visit and treatment group within cohort.

9.7. Concomitant Medications

Prior and concomitant medications will be summarized descriptively by treatment within cohort, Anatomical Therapeutic Chemical (ATC) Class Level 4, and Preferred Term using counts and percentages.

Prior medications will be presented separately from concomitant medications. Medications that started before the first application of IP will be considered prior medications whether or not they were stopped before the first application of study drug. Any medications continuing or starting after the first application of study drug will be considered to be concomitant. If a medication starts before the first application of study drug and continues after the first application of study drug it will be considered both prior and concomitant.

9.8. Modified Total Lesion Symptom Score (mTLSS)

The modified Total Lesion Symptom Score (mTLSS) is used to determine the intensity of features as part of the IGA Severity Score. The total mTLSS is calculated as the sum of scores (0 = absent, 1 = mild, 2 = moderate, 3 = severe) assigned by the investigator for the chronic hand eczema parameters.

This endpoint was removed from the protocol as of amendment 1 (11May2020), thus a limited number of subjects and visits had data collected. The mTLSS results will be listed only.

10. CHANGES FROM PLANNED ANALYSIS

The following analysis populations have been added:

- The PRU4 population has been added to facilitate WI-NRS analysis on the ITT population;
- The PNRS4, PNRS3, and PNRS2 populations have been added to facilitate Pain NRS analysis for subjects achieving a 4-point, 3-point, and 2-point reduction from baseline, respectively; and
- The All Treatment population has been added to facilitate Cohort 1 efficacy analyses.
- The ND population has been added to facilitate Cohort 2 analyses of nail dystrophy.

These populations are not included in the protocol.

The exploratory endpoint is change from baseline in nail dystrophy; since no baseline measurement will be collected for millimeters of normal nail distal to cuticle, it will be assumed that the amount of normal nail at baseline is 0 mm.

The definition of compliance was updated to exclude subjects who missed more than 3 consecutive days of dosing, versus subjects who missed more than 3 consecutive doses.

The following secondary endpoints were added upon request by the Sponsor:

- The rate of achievement of IGA of "clear" or "almost clear" PLUS at least a 2-point improvement from Baseline at Week 13
- The rate of achievement of at least a 2-point improvement from baseline at Week 13
- The rate of achievement of IGA of "clear" or "almost clear" at Week 13
- Change in IGA score at Week 13 as compared to baseline
- Change in WI-NRS pruritus score at 1, 3, 5, 6, 7, 9, 10, 11, and 13 compared to baseline (Weeks 2, 4, 8, and 12 were already included)
- Percent change in WI-NRS pruritus score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug compared to baseline
- Change and percent change in HECSI score at Weeks 2, 4, 8, 12, and 13 compared to baseline
- Achievement of HECSI-75
- Percent change in Pain NRS score from Baseline to at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug
- The rate of achievement of ≥3-point reduction from baseline in Pain NRS score at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug in subjects with baseline Pain NRS score of at least 3
- The rate of achievement of ≥2-point reduction from baseline in Pain NRS score 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 weeks after first application of study drug weeks in subjects with baseline Pain NRS score of at least 2

- Percent change from baseline in QOLHEQ score at each visit

The following treatment comparisons were added:

- ARQ-252 cream (all strengths and dose frequencies) versus vehicle cream (all dose frequencies)
- ARQ-252 cream 0.3% (all dose frequencies) versus vehicle cream (all dose frequencies)

For all efficacy treatment comparisons, vehicle cream will be pooled for analysis over both dose frequencies.

Efficacy analysis for Cohort 1 was not specified in the protocol, however, upon request from Sponsor, all efficacy data collected for Cohort 1 (IGA, HECSI, average weekly WI-NRS, average weekly Pain NRS, and % BSA affected by disease) will be summarized.

Subgroup analyses for IGA Success by study site (Week 12 only) and by baseline IGA severity were added.

An analysis of HECSI-75 and total % BSA affected by disease were also requested to be added.

All analyses of time to event (i.e., time to IGA of "clear" or "almost clear"; time to the first achievement of ≥4-point reduction from Baseline in WI-NRS pruritus score in subjects with Baseline WI-NRS pruritus score of at least 4; and time to the first achievement of ≥4-point reduction from Baseline in Pain NRS score in subjects with Baseline Pain NRS score of at least 4) were removed at the request of the sponsor.

11. OTHER PLANNED ANALYSIS

11.1. Pharmacokinetic Analysis

All PK collection information from the eCRF will be presented in a listing. Concentration data and PK parameters will be summarized by time point (concentration data), study visit, and treatment group within cohort using summary statistics. In addition, PK concentration and parameter listings will be presented.

12. REFERENCES

ASA. (2018) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2018. http://www.amstat.org/about/ethicalguidelines.cfm

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RSS. (2014) The Royal Statistical Society: Code of Conduct, 2014. https://rss.org.uk/about/policy-and-guidelines/code-of-conduct/

Ratitch, B., Lipkovich, I., & O'Kelly, M. (2013). *Combining Analysis Results from Multiply Imputed Categorical Data*. PharmaSUG. https://www.pharmasug.org/proceedings/2013/SP/PharmaSUG-2013-SP03.pdf

13. TABLES, LISTINGS, AND FIGURES

All TLFs will have a header showing the sponsor company name and protocol and a footer showing the version of SAS, the file name and path, and the source of the data (e.g., listing number).

13.1. Planned Table Descriptions

The following are planned summary tables for protocol number ARQ-252-205. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

13.1.1. Demographic Data

Table 8: Demographic Data Summary Tables and Figures

Table Number	Population	Table Title / Summary
Table 14.1.1	All Randomized	Cohorts 1 and 2: Summary of Subject Disposition
Table 14.1.2.1	Safety	Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Table 14.1.2.2	ITT	Cohort 2: Summary of Demographics and Baseline Characteristics
Table 14.1.3.1	Safety	Cohorts 1 and 2: Summary of Medical History by System Organ Class and Preferred Term
Table 14.1.3.2	Safety	Cohorts 1 and 2: Summary of Chronic Hand Eczema Medical History
Table 14.1.4	Safety	Cohorts 1 and 2: Summary of Protocol Deviations
Table 14.1.5	Safety	Cohorts 1 and 2: Summary of Prior Medications by ATC Class Level 4 and Preferred Term
Table 14.1.6	Safety	Cohorts 1 and 2: Summary of Study Drug Exposure and Compliance

13.1.2. Efficacy Data

Table 9: Efficacy Data

Table Number	Population	Table Title / Summary
Table 14.2.1.1.1	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.1.2	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.2.1	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data Categorical Results
Table 14.2.1.2.2	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data Categorical Results
Table 14.2.1.2.3	PP	Cohort 2: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data Categorical Results
Table 14.2.1.2.4	PP	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data Categorical Results
Table 14.2.1.2.5	All Treated	Cohort 1: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data Categorical Results
Table 14.2.1.3.1	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.3.2	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.3.3	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Multiple Imputation Categorical Results

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.1.3.4	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Multiple Imputation Categorical Results
Table 14.2.1.3.5	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data Categorical Results
Table 14.2.1.3.6	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data Categorical Results
Table 14.2.1.3.7	PP	Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data Categorical Results
Table 14.2.1.3.8	PP	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data Categorical Results
Table 14.2.1.3.9	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Observed Data Categorical Results
Table 14.2.1.3.10	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Observed Data Categorical Results
Table 14.2.1.3.11	ITT	Cohort 2: Summary of Proportion of Subjects Achieving Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) at Week 12 by Study Site – Observed Data Categorical Results
Table 14.2.1.3.12	ITT	Cohort 2, Pooled Treatments: Summary of Proportion of Subjects Achieving Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) at Week 12 by Study Site – Observed Data Categorical Results

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.1.3.13	All Treated	Cohort 1: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data Categorical Results
Table 14.2.1.4.1	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.4.2	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Multiple Imputation Categorical Results
Table 14.2.1.4.3	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data Categorical Results
Table 14.2.1.4.4	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data Categorical Results
Table 14.2.1.4.5	All Treated	Cohort 1: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data Categorical Results
Table 14.2.1.5.1	ITT	Cohort 2: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation
Table 14.2.1.5.2	ITT	Cohort 2, Pooled Treatments: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation
Table 14.2.1.5.3	ITT	Cohort 2: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
Table 14.2.1.5.4	ITT	Cohort 2, Pooled Treatments: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
Table 14.2.1.5.5	All Treated	Cohort 1: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
Table 14.2.1.6.1	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation – ANCOVA
Table 14.2.1.6.2	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation – ANCOVA

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.1.6.3	ITT	Cohort 2: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
Table 14.2.1.6.4	ITT	Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
Table 14.2.1.6.5	All Treated	Cohort 1: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
Table 14.2.2.1.1	ITT	Cohort 2: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit
Table 14.2.2.1.2	ITT	Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit
Table 14.2.2.1.3	ITT	Cohort 2: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit – ANCOVA
Table 14.2.2.1.4	ITT	Cohort 2, Pooled Treatments: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit – ANCOVA
Table 14.2.2.1.5	PP	Cohort 2: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit – ANCOVA
Table 14.2.2.1.6	PP	Cohort 2, Pooled Treatments: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit – ANCOVA
Table 14.2.2.1.7	PRU4	Cohort 2: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.1.8	PRU4	Cohort 2, Pooled Treatments: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.1.9	All Treated	Cohort 1: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit
Table 14.2.2.1.10	All Treated	Cohort 1: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Scores by Study Visit – ANCOVA
Table 14.2.2.1.11	PRU4	Cohort 1: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.2.1	ITT	Cohort 2: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.2.2.2	ITT	Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit
Table 14.2.2.2.3	ITT	Cohort 2: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
Table 14.2.2.2.4	ITT	Cohort 2, Pooled Treatments: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
Table 14.2.2.2.5	PP	Cohort 2: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
Table 14.2.2.2.6	PP	Cohort 2, Pooled Treatments: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
Table 14.2.2.2.7	ITT	Cohort 2: Summary of Achievement of HECSI-75 by Study Visit
Table 14.2.2.2.8	ITT	Cohort 2, Pooled Treatments: Summary of Achievement of HECSI-75 by Study Visit
Table 14.2.2.2.9	PP	Cohort 2: Summary of Achievement of HECSI-75 by Study Visit
Table 14.2.2.2.10	PP	Cohort 2, Pooled Treatments: Summary of Achievement of HECSI-75 by Study Visit
Table 14.2.2.2.11	All Treated	Cohort 1: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit
Table 14.2.2.2.12	All Treated	Cohort 1: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
Table 14.2.2.3.1	ITT	Cohort 2: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit
Table 14.2.2.3.2	ITT	Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit
Table 14.2.2.3.3	ITT	Cohort 2: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit – ANCOVA
Table 14.2.2.3.4	ITT	Cohort 2, Pooled Treatments: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit – ANCOVA
Table 14.2.2.3.5	PNRS4	Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.6	PNRS4	Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.7	PNRS3	Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Visit

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.2.3.8	PNRS3	Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.9	PNRS2	Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.10	PNRS2	Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.11	All Treated	Cohort 1: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit
Table 14.2.2.3.12	All Treated	Cohort 1: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Visit – ANCOVA
Table 14.2.2.3.13	PNRS4	Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.14	PNRS3	Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Visit
Table 14.2.2.3.15	PNRS2	Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Visit
Table 14.2.2.4.1	ITT	Cohort 2: Summary and Change and Percent Change from Baseline in Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit
Table 14.2.2.4.2	ITT	Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit
Table 14.2.2.4.3	ITT	Cohort 2: Summary of Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Total Score by Study Visit – ANCOVA
Table 14.2.2.4.4	ITT	Cohort 2, Pooled Treatments: Summary of Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Total Score by Study Visit – ANCOVA
Table 14.2.2.5.1	ITT	Cohort 2: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
Table 14.2.2.5.2	ITT	Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
Table 14.2.2.5.3	ITT	Cohort 2: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA
Table 14.2.2.5.4	ITT	Cohort 2, Pooled Treatments: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA

Table 9: Efficacy Data (Continued)

Table Number	Population	Table Title / Summary
Table 14.2.2.5.5	All Treated	Cohort 1: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
Table 14.2.2.5.6	All Treated	Cohort 1: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA
Table 14.2.3.1	ND	Cohort 2: Summary of Nail Dystrophy Normal-Appearing Nail Distal to Cuticle (mm) by Study Visit
Table 14.2.3.2	ND	Cohort 2, Pooled Treatments: Summary of Nail Dystrophy Normal-Appearing Nail Distal to Cuticle (mm) by Study Visit

13.1.3. Safety Data

13.1.3.1. Displays of Adverse Events

Table 10: Safety Data

Table Number	Population	Table Title / Summary
Table 14.3.1.1	Safety	Cohorts 1 and 2: Summary of Treatment Emergent Adverse Events
Table 14.3.1.2	Safety	Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Table 14.3.1.3	Safety	Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Table 14.3.1.4	Safety	Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug
Table 14.3.1.5	Safety	Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term
Table 14.3.1.6	Safety	Cohorts 1 and 2: Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term
Table 14.3.1.7	Safety	Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term
Table 14.3.1.8	Safety	Cohorts 1 and 2: Incidence of Related Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity

13.1.3.2. Summary of Deaths, Other Serious and Significant Adverse Events

Table Number	Population	Table Title / Summary
Table 14.3.2.1	Safety	Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class and Preferred Term
Table 14.3.2.2	Safety	Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Table 14.3.2.3	Safety	Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug

13.1.3.3. Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events

Table Number	Population	Table Title / Summary
Table 14.3.3.1	Safety	Listing of Adverse Events Leading to Study Drug Discontinuation
Table 14.3.3.2	Safety	Listing of Serious Adverse Events
Table 14.3.3.3	Safety	Listing of Deaths

13.1.3.4. Abnormal Laboratory Values

Table Number	Population	Table Title / Summary
NA		

13.1.3.5. Laboratory Data Summary Tables

Table Number	Population	Table Title / Summary
Table 14.3.5.1.1.1	Safety	Cohort 1: Summary of Serum Chemistry Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.1.1.2	Safety	Cohort 2: Summary of Serum Chemistry Laboratory Results (Standard Units) by Study Visit – Cohort 2
Table 14.3.5.1.2.1	Safety	Cohort 1: Shift from Baseline in Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.1.2.2	Safety	Cohort 2: Shift from Baseline in Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.2.1.1	Safety	Cohort 1: Summary of Hematology Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.2.1.2	Safety	Cohort 2: Summary of Hematology Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.2.2.1	Safety	Cohort 1: Shift from Baseline in Hematology Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.2.2.2	Safety	Cohort 2: Shift from Baseline in Hematology Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.3.1.1	Safety	Cohort 1: Summary of Quantitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.3.1.2	Safety	Cohort 2: Summary of Quantitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.3.2.1	Safety	Cohort 1: Shift from Baseline in Quantitative and Qualitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.3.2.2	Safety	Cohort 2: Shift from Baseline in Quantitative and Qualitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Table 14.3.5.3.3.1	Safety	Cohort 1: Summary of Qualitative Urinalysis Laboratory Results by Study Visit
Table 14.3.5.3.3.2	Safety	Cohort 2: Summary of Qualitative Urinalysis Laboratory Results by Study Visit

13.1.3.6. Other Safety Data Summary Tables

Table Number	Population	Table Title / Summary
Table 14.3.6.1.1	Safety	Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit
Table 14.3.6.1.2	Safety	Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit Categorical Results
Table 14.3.6.1.3	Safety	Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Other Effects) by Study Visit Categorical Results
Table 14.3.6.2.1	Safety	Cohorts 1 and 2: Summary of Subject Local Tolerability Assessment by Study Visit
Table 14.3.6.2.2	Safety	Cohorts 1 and 2: Summary of Subject Local Tolerability Assessment by Study Visit Categorical Results
Table 14.3.6.3.1	Safety	Cohort 1: Summary of Vital Signs by Study Visit
Table 14.3.6.3.2	Safety	Cohort 2: Summary of Vital Signs by Study Visit
Table 14.3.6.4.1.1	Safety	Cohort 1: Summary of 12-Lead Electrocardiogram by Study Visit
Table 14.3.6.4.1.2	Safety	Cohort 2: Summary of 12-Lead Electrocardiogram by Study Visit
Table 14.3.6.4.2.1	Safety	Cohort 1: Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Table 14.3.6.4.2.2	Safety	Cohort 2: Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Table 14.3.6.5.1	Safety	Cohort 1: Summary of Physical Examination by Study Visit
Table 14.3.6.5.2	Safety	Cohort 2: Summary of Physical Examination by Study
Table 14.3.6.6	Safety	Cohorts 1 and 2: Summary of Concomitant Medications by ATC Class Level 4 and Preferred Term

13.1.4. Pharmacokinetic Data

13.1.4.1. Pharmacokinetic Data Summary Tables

Table 11: Pharmacokinetic Data

Table Number	Population	Table Title / Summary
Table 14.4.1.1	PK	Cohort 1: Summary of Pharmacokinetic Results by Study Visit and Time Point
Table 14.4.1.2	PK	Cohort 2: Summary of Pharmacokinetic Results by Study Visit and Time Point
Table 14.4.2	PK	Cohort 1: Summary of Pharmacokinetic Parameters by Study Visit

13.2. Planned Listing Descriptions

The following are planned data and patient/subject data listings for protocol number ARQ-252-205.

In general, one listing will be produced per CRF domain. All listings will be sorted by treatment, site, and subject number. All calculated variables will be included in the listings. Screen failures will only be presented in Listing 16.2.2.1.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages.

Table 12: Planned Listings

16.2.1 Subject Discontinuations/Completions

Listing Number	Population	Title
Listing 16.2.1.1	All Subjects	Subject Disposition
Listing 16.2.1.2	All Subjects	Subject Visits

16.2.2 Protocol Deviations

Listing Number	Population	Title
Listing 16.2.2.1	All Subjects	Inclusion and Exclusion Criteria Not Met
Listing 16.2.2.2	All Subjects	Protocol Deviations

16.2.3 Subjects Excluded from the Efficacy Analyses

Listing Number	Population	Title
Listing 16.2.3.1	All Subjects	Subject Randomization
Listing 16.2.3.2	All Subjects	Analysis Populations

16.2.4 Demographic Data and Other Baseline Characteristics

Listing Number	Population	Title
Listing 16.2.4.1.1	All Subjects	Subject Demographics
Listing 16.2.4.1.2	All Subjects	Baseline Characteristics
Listing 16.2.4.2.1	All Subjects	Medical History
Listing 16.2.4.2.2	All Subjects	Chronic Hand Eczema Medical History

16.2.5 Compliance and/or Drug Concentration Data

Listing Number	Population	Title
Listing 16.2.5.1	All Subjects	Study Drug Application at the Study Site
Listing 16.2.5.2	All Subjects	Study Drug Accountability
Listing 16.2.5.3	All Subjects	Diary Dispensation
Listing 16.2.5.4	All Subjects	Compliance (CRF)
Listing 16.2.5.5.1	All Subjects	Study Drug Interruption (QD)
Listing 16.2.5.5.2	All Subjects	Study Drug Interruption (BID)
Listing 16.2.5.6.1	PK	Cohort 1: Pharmacokinetic Sample Collection
Listing 16.2.5.6.2	PK	Cohort 2: Pharmacokinetic Sample Collection
Listing 16.2.5.7	PK	Cohort 1: Pharmacokinetic Calculated Parameters

16.2.6 Individual Efficacy Response Data

Listing Number	Population	Title
Listing 16.2.6.1	All Subjects	Investigator Global Assessment (IGA)
Listing 16.2.6.2	All Subjects	Worst Itch Numerical Rating Scale (WI-NRS)
Listing 16.2.6.3	All Subjects	Hand Eczema Severity Index (HECSI)
Listing 16.2.6.4	All Subjects	Pain Numeric Rating Scale (NRS)
Listing 16.2.6.5	All Subjects	Quality of Life in Hand Eczema Questionnaire (QOLHEQ)
Listing 16.2.6.6	All Subjects	Body Surface Area (BSA)
Listing 16.2.6.7	All Subjects	Nail Dystrophy Assessment

16.2.7 Adverse Event Listings (by Subject)

Listing Number	Population	Title
Listing 16.2.7.1	All Subjects	Adverse Events

16.2.8 Laboratory Values (by Subject)

Listing Number	Population	Title
Listing 16.2.8.1.1	All Subjects	Clinical Laboratory Data: Clinical Chemistry
Listing 16.2.8.1.2	All Subjects	Clinical Laboratory Data: Hematology
Listing 16.2.8.1.3	All Subjects	Clinical Laboratory Data: Urinalysis
Listing 16.2.8.1.4	All Subjects	Clinical Laboratory Data: TSH/T4
Listing 16.2.8.1.5	Female Subjects	Clinical Laboratory Data: Serum and Urine Pregnancy Test
Listing 16.2.8.1.6	Female Subjects	Follicle Stimulating Hormone Test

16.2.9 Other Clinical Observations and Measurements (by Subject)

Listing Number	Population	Title
Listing 16.2.9.1	All Subjects	Investigator Local Tolerability Assessments
Listing 16.2.9.2	All Subjects	Subject Local Tolerability Assessments
Listing 16.2.9.3	All Subjects	Vital Signs
Listing 16.2.9.4	All Subjects	12-Lead Electrocardiogram (ECG)
Listing 16.2.9.5	All Subjects	Physical Examination
Listing 16.2.9.6	All Subjects	Medical Photography
Listing 16.2.9.7	All Subjects	Prior and Concomitant Medications
Listing 16.2.9.8.1	All Subjects	Hand Washing/Hand Sanitizer Use (QD Dosing)
Listing 16.2.9.8.2	All Subjects	Hand Washing/Hand Sanitizer Use (BID Dosing)
Listing 16.2.9.9	All Subjects	Modified Total Lesion Symptom Score (mTLSS)

14. TABLES, LISTINGS, AND LISTING SHELLS

14.1. Standard Layout for all Tables, Listings, and Figures

The following standard layout will be applied to all Tables, Listings, and Figures (TLFs) in support of this study. Note that programming notes may be added if appropriate after each TLF shell.

Figure 1: Standardized Layout

Arcutis Biotherapeutics, Inc.	CONFIDENTIAL	Page xx of xx
Protocol ARQ-252-205		<Version>

<Table, Listing, Figure> xx.x.x

<Title of Table Listing or Figure>

<Study Population and if applicable subgroup Description>

Body of Table, Listing or Figure

<Abbreviations: XXX = xxxxx; YYY = yyyyy.>

<Note: If directly Applicable>

Footnote 1 *<if applicable>* Recommendation is to keep footnotes to a minimum

Footnote 2 *<if applicable>*

Footnote n *<if applicable>*

\\statsdrive.premier-research.com\stats$\Arcutis\ARQ-252\ARQ-252-205\Analysis\Tables\<version>\<pgm name>.sas

Executed on DDMONYYYY at hh:mm on data from DDMONYYYY using SAS Version 9.4

14.2. Planned Table Shells

Table 14.1.1
Cohorts 1 and 2: Summary of Subject Disposition
All Randomized Subjects

	Cohort 1	Cohort 2				
Status	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Study Populations:						
ITT Population [1]	--	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Safety Population [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PP Population [3]	--	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PRU4 Population [4]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PNRS4 Population [5]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PNRS3 Population [6]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PNRS2 Population [7]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ND Population [8]	--	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PK Population [9]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
All Treated Population [10]	XX (XX.X%)	--	--	--	--	--

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; ITT = Intent-to-treat; ND = nail dystrophy; NRS = Numeric Rating Scale; PNRS2 = Subjects with Pain NRS Score ≥2 at Baseline; PNRS3 = Subjects with Pain NRS Score ≥3 at Baseline; PNRS4 = Subjects with Pain NRS Score ≥4 at Baseline; PP = per protocol; PRU4 = Subjects with WI-NRS Pruritus Score ≥4 at Baseline; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects enrolled (Cohort 1) or randomized (Cohort 2) within planned treatment and overall*100.
[1] The ITT population includes all subjects randomized to Cohort 2.
[2] The Safety population includes all subjects who are enrolled (Cohort 1) or randomized (Cohort 2) and received at least 1 confirmed dose of investigational product.
[3] The PP population includes all subjects in the Safety population in Cohort 2, who were at least 80% compliant with study medication application, and showed no important deviations from the study protocol that would affect the interpretation of efficacy.
[4] The PRU4 population is a subset of the ITT population and includes subjects with WI-NRS pruritus score ≥4 at baseline.
[5] The PNRS4 population is a subset of the ITT population and includes subjects with Pain NRS score ≥4 at baseline.
[6] The PNRS3 population is a subset of the ITT population and includes subjects with Pain NRS score ≥3 at baseline.
[7] The PNRS2 population is a subset of the ITT population and includes subjects with Pain NRS score ≥2 at baseline.
[8] The ND population is a subset of the ITT population and includes subjects with nail dystrophy at baseline.
[9] The PK population includes all subjects receiving the active drug with sufficient plasma concentrations of ARQ-254 to define a profile, as determined by the pharmacokineticist.
[10] The All Treated Population includes all subjects in the Safety population in Cohort 1.
Reference Listings: 16.2.1.1, 16.2.3.2

Table 14.1.1 (cont.)
Cohorts 1 and 2: Summary of Subject Disposition
All Randomized Subjects

	Cohort 1	Cohort 2				
Status	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Completed Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ongoing in Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Prematurely Discontinued from Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Withdrawal by Subject	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sponsor's Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Physician Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Compliance	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Protocol Violation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lost to Follow-up	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Adverse Event	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Death	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pregnancy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; ITT = Intent-to-treat; ND = nail dystrophy; NRS = Numeric Rating Scale; PNRS2 = Subjects with Pain NRS Score ≥2 at Baseline; PNRS3 = Subjects with Pain NRS Score ≥3 at Baseline; PNRS4 = Subjects with Pain NRS Score ≥4 at Baseline; PP = per protocol; PRU4 = Subjects with WI-NRS Pruritus Score ≥4 at Baseline; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects enrolled (Cohort 1) or randomized (Cohort 2) within planned treatment and overall*100.
[1] The ITT population includes all subjects randomized to Cohort 2.
[2] The Safety population includes all subjects who are enrolled (Cohort 1) or randomized (Cohort 2) and received at least 1 confirmed dose of investigational product.
[3] The PP population includes all subjects in the Safety population in Cohort 2, who were at least 80% compliant with study medication application, and showed no important deviations from the study protocol that would affect the interpretation of efficacy.
[4] The PRU4 population is a subset of the ITT population and includes subjects with WI-NRS pruritus score ≥4 at baseline.
[5] The PNRS4 population is a subset of the ITT population and includes subjects with Pain NRS score ≥4 at baseline.
[6] The PNRS3 population is a subset of the ITT population and includes subjects with Pain NRS score ≥3 at baseline.
[7] The PNRS2 population is a subset of the ITT population and includes subjects with Pain NRS score ≥2 at baseline.
[8] The ND population is a subset of the ITT population and includes subjects with nail dystrophy at baseline.
[9] The PK population includes all subjects receiving the active drug with sufficient plasma concentrations of ARQ-254 to define a profile, as determined by the pharmacokineticist.
[10] The All Treated Population includes all subjects in the Safety population in Cohort 1.
Reference Listings: 16.2.1.1, 16.2.3.2

Table 14.1.1 (cont.)
Cohorts 1 and 2: Summary of Subject Disposition
All Randomized Subjects

Status	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)
Prematurely Discontinued from Study Due to COVID-19 Disruption	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Withdrawal by Subject	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sponsor's Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Physician Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Compliance	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Protocol Violation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lost to Follow-up	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Adverse Event	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Death	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pregnancy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; ITT = Intent-to-treat; ND = nail dystrophy; NRS = Numeric Rating Scale; PNRS2 = Subjects with Pain NRS Score ≥2 at Baseline; PNRS3 = Subjects with Pain NRS Score ≥3 at Baseline; PNRS4 = Subjects with Pain NRS Score ≥4 at Baseline; PP = per protocol; PRU4 = Subjects with WI-NRS Pruritus Score ≥4 at Baseline; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects enrolled (Cohort 1) or randomized (Cohort 2) within planned treatment and overall*100.
[1] The ITT population includes all subjects randomized to Cohort 2.
[2] The Safety population includes all subjects who are enrolled (Cohort 1) or randomized (Cohort 2) and received at least 1 confirmed dose of investigational product.
[3] The PP population includes all subjects in the Safety population in Cohort 2, who were at least 80% compliant with study medication application, and showed no important deviations from the study protocol that would affect the interpretation of efficacy.
[4] The PRU4 population is a subset of the ITT population and includes subjects with WI-NRS pruritus score ≥4 at baseline.
[5] The PNRS4 population is a subset of the ITT population and includes subjects with Pain NRS score ≥4 at baseline.
[6] The PNRS3 population is a subset of the ITT population and includes subjects with Pain NRS score ≥3 at baseline.
[7] The PNRS2 population is a subset of the ITT population and includes subjects with Pain NRS score ≥2 at baseline.
[8] The ND population is a subset of the ITT population and includes subjects with nail dystrophy at baseline.
[9] The PK population includes all subjects receiving the active drug with sufficient plasma concentrations of ARQ-254 to define a profile, as determined by the pharmacokineticist.
[10] The All Treated Population includes all subjects in the Safety population in Cohort 1.
Reference Listings: 16.2.1.1, 16.2.3.2

Table 14.1.2.1
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Age (years)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Gender							
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Child-Bearing Potential? [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ethnicity							
Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety Population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Race							
American-Indian or Alaska Native	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Asian	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Black or African-American	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Native Hawaiian or Other Pacific Islander	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
White	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
More than One Race	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Height (cm)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Weight (kg)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Body Mass Index (kg/m^2)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Body Surface Area (%) Affected by Disease							
Dorsal (Left Hand)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Dorsal (Right Hand)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Palmar (Left Hand)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Palmar (Right Hand)							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Body Surface Area (%) Affected by Disease (cont.)							
Total Hand							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline IGA							
Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Almost Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline IGA - Numeric							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline WI-NRS - Numeric [2]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline WI-NRS [2]							
0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
8	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
9	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
10	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline HECSI Fingertips Subscore (range 0-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Fingertips Subscore, where subscore > 0 (range 1-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Fingers (Except Tips) Subscore (range 0-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Fingers (Except Tips) Subscore, where subscore > 0 (range 1-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline HECSI Palm of Hands Subscore (range 0-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Palm of Hands Subscore, where subscore > 0 (range 1-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Back of Hands Subscore (range 0-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Back of Hands Subscore, where subscore > 0 (range 1-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline HECSI Wrists Subscore (range 0-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Wrists Subscore, where subscore > 0 (range 1-72) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline HECSI Total Score (range 0-360) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline Pain NRS - Numeric [4]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline Pain NRS [4]							
0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
8	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
9	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
10	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline QOLHEQ Symptoms Subscore (range 0-27) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline QOLHEQ Emotions Subscore (range 0-31) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline QOLHEQ Functioning Subscore (range 0-32) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Baseline QOLHEQ Treatment and Prevention Subscore (range 0-27) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.1 (cont.)
Cohorts 1 and 2: Summary of Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)	Overall (N=XXX)
Baseline QOLHEQ Total Score (range 0-117) [3]							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Presence of Nail Dystrophy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Nail with Worst Dystrophy							
Left	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; NRS = numeric rating scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within overall (Cohort 1) or treatment received (Cohort 2)*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety population.
[2] The WI-NRS was determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[3] Lower scores indicate better outcomes.
[4] The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours. The scale is from 0 to 10, which ranges from "no pain" to "worst possible pain".
Reference Listings: 16.2.4.1.1, 16.2.4.1.2, 16.2.6.1, 16.2.6.2, 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7

Table 14.1.2.2
Cohort 2: Summary of Demographics and Baseline Characteristics
ITT Population

(Same shell as Table 14.1.2.1; only display Cohort 2 treatments; replace first footnote with "Note: Percentages are n/Number of subjects in the ITT population planned treatment *100.")

Table 14.1.3.1
Cohorts 1 and 2: Summary of Medical History by System Organ Class and Preferred Term
Safety Population

	Cohort 1	Cohort 2				
System Organ Class Preferred Term	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Subjects with at least 1 Recorded Medical History	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; PT = preferred term; QD = once daily; SOC = system organ class.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received*100. Medical histories were coded using MedDRA version 23.0. Subjects were counted once for each SOC and once for each PT. Medical history terms are displayed by descending frequency of SOC over all subjects, then PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.4.2.1, 16.2.4.2.2

Table 14.1.3.2
Cohorts 1 and 2: Summary of Chronic Hand Eczema Medical History
Safety Population

Category	Cohort 1	Cohort 2				
	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Morphologic Subtype of Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Chronic Fissured Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Recurrent Vesicular Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Hyperkeratotic Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pulpitis	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Interdigital Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Nummular Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unclassified Hand Eczema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patch Test Results [1]						
Positive	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Negative	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Tested/Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Distribution of Chronic Hand Eczema						
Palmar (including lateral aspects of fingers)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Left Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Dorsal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Left Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Interdigital	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Left Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pulpitis	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Left Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right Hand	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received*100.
[1] Includes results from if the subject has ever been patched tested and results from the past 3 years. If a subject has results from both patch test questions, the worst case is presented here.
Reference Listings: 16.2.4.2.1, 16.2.4.2.2

Table 14.1.4
Cohorts 1 and 2: Summary of Protocol Deviations
Safety Population

Category	Cohort 1	Cohort 2				
	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Subjects with Any Protocol Deviations	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with Any Protocol Deviations Related to COVID-19 Disruption	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with Important Protocol Deviations	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received*100. Only important protocol deviations are presented. Subjects with Any Protocol Deviations row can include counts from important and not important deviations. Subjects with one or more deviations within a type of protocol deviation were counted only once. Protocol Deviations were collected throughout the study.
Reference Listing: 16.2.2.2

Table 14.1.5
Cohorts 1 and 2: Summary of Prior Medications by ATC Class Level 4 and Preferred Term
Safety Population

ATC Class Level 4 Preferred Term	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Subjects with at least 1 Prior Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: ATC = Anatomic Therapeutic Chemical; BID = twice daily; PT = preferred term; QD = once daily; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Medications were coded using WHO-DDE Global B3 version September 2019. Prior medications are all medications that were started before the application of study drug. Medications are displayed by alphabetical order of ATC Level 4 classification, then descending frequency of PT within ATC, and then alphabetically by PT. Subjects were counted only once for each ATC and PT.
[1] ATC Level 4 was not definable for these preferred terms due to multiple ingredients that cannot be mapped to an ATC Level 4 term, route of administration and indication that is not defined in an ATC Level 4 term, or some similar circumstance.
Reference Listing: 16.2.9.7

Programming note: *ATC & PT text should be presented as is from the dataset. If medications are coded but are missing ATC Class Level 4, display as "NOT DEFINED [1]" in the ATC Class Level 4 row and include footnote [1]; otherwise remove footnote [1] from the table.*

Table 14.1.6
Cohorts 1 and 2: Summary of Study Drug Exposure and Compliance
Safety Population

Variable Statistic / Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Total Number of IP Applications						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Total Weight of IP Applied (g) [1]						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Compliance [2]						
>100%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥ 80% - ≤100%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
< 80%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 3 Consecutive Missed Days	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Compliant [3]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; IP = investigational product; QD = once daily.
Note: n is the number of subjects in the Safety Population. Percentages are n/Number of subjects in the Safety Population within treatment received*100.
[1] Total weight of IP is determined by subtracting returned tube weight from the dispensed tube weight.
[2] Compliance is calculated based on number of applications divided by the expected number of IP applications for each subject*100.
[3] A subject is considered compliant if the subject applies at least 80% of the expected applications during the IP application period and does not miss more than 3 consecutive days of dosing (3 doses for QD and 6 doses for BID).
Reference Listings: 16.2.5.1, 16.2.5.2, 16.2.5.4

Table 14.2.1.1.1
Cohort 2: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Multiple Imputation
Categorical Results
ITT Population

	Cohort 2			
Study Visit Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Baseline	XX	XX	XX	XX
0 = Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2	XX	XX	XX	XX
0 = Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
IGA Score of "Clear" or "Almost Clear" [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: The grades and success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).

Reference Listing: 16.2.6.1

Table 14.2.1.1.2
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Multiple Imputation
Categorical Results
ITT Population

Study Visit Category/Statistic	Cohort 2 ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	 ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Baseline	XX	XX	XX
0 = Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2	XX	XX	XX
0 = Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
IGA Score of "Clear" or "Almost Clear" [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: The grades and success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.2.1
Cohort 2: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.1.1; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.2.2
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.1.2; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.2.3
Cohort 2: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Observed Data
Categorical Results
PP Population

(Same shell as Table 14.2.1.1.1; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.2.4
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades and Score of "Clear" or "Almost Clear" by Study Visit – Observed Data
Categorical Results
PP Population

(Same shell as Table 14.2.1.1.2; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.2.5
Cohort 1: Summary of Investigator Global Assessment (IGA) Grades Score of "Clear" or "Almost Clear" by Study Visit – Observed Data
Categorical Results
All Treated Population

Study Visit Category/Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Baseline	XX
0 = Clear	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)
2 = Mild	XX (XX.X%)
3 = Moderate	XX (XX.X%)
4 = Severe	XX (XX.X%)
Week 2	XX
0 = Clear	XX (XX.X%)
1 = Almost Clear	XX (XX.X%)
2 = Mild	XX (XX.X%)
3 = Moderate	XX (XX.X%)
4 = Severe	XX (XX.X%)
IGA Score of "Clear" or "Almost Clear" [1]	
Yes	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)
No	XX (XX.X%)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the All Treated population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.1

Table 14.2.1.3.1
Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Multiple Imputation
Categorical Results
ITT Population

	Cohort 2			
Study Visit Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX	XX
IGA Success [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.2
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Multiple Imputation
Categorical Results
ITT Population

	Cohort 2		
Study Visit Category/Statistic	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX
IGA Success [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.3
Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Multiple Imputation
Categorical Results
ITT Population

Baseline IGA Score = X

	Cohort 2			
Study Visit Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX	XX
IGA Success [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit and subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success plus ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.4
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Multiple Imputation
Categorical Results
ITT Population

Baseline IGA Score = X

	Cohort 2		
Study Visit Category/Statistic	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX
IGA Success [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit and subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success plus ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.5
Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.3.1; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.6
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.3.2; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.7
Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline)
by Study Visit – Observed Data
Categorical Results
PP Population

(Same shell as Table 14.2.1.3.1; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.8
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline)
by Study Visit – Observed Data
Categorical Results
PP Population

(Same shell as Table 14.2.1.3.2; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.9
Cohort 2: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.3.3; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NE = not estimable; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit and subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.10
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit and Baseline IGA Score – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.3.4; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; NE = not estimable.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit and subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.3.11
Cohort 2: Summary of Proportion of Subjects Achieving Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) at Week 12 by Study Site – Observed Data
Categorical Results
ITT Population

	Cohort 2			
Study Site	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
SITENAME1 (Site SITEID1)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME2 (Site SITEID2)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME3 (Site SITEID3)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME4 (Site SITEID4)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME5 (Site SITEID5)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME6 (Site SITEID6)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
…				

Abbreviations: BID = twice daily; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at Week 12 for each subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. IGA Success is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline.
Reference Listing: 16.2.6.1

Programming note: *for the first column, use the site name (SITENAM variable) and site number (SITEID variable), e.g, "DermEffects (Site 103)".*

Table 14.2.1.3.12
Cohort 2, Pooled Treatments: Summary of Proportion of Subjects Achieving Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) at Week 12 by Study Site – Observed Data
Categorical Results
ITT Population

	Cohort 2		
Study Site	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
SITENAME1 (Site SITEID1)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME2 (Site SITEID2)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME3 (Site SITEID3)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME4 (Site SITEID4)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME5 (Site SITEID5)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
SITENAME6 (Site SITEID6)	XX/XX (XX.X%)	XX/XX (XX.X%)	XX/XX (XX.X%)
…			

Abbreviation: IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at Week 12 for each subgroup*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. IGA Success is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline
Reference Listing: 16.2.6.1

Programming note: *for the first column, use the site name (SITENAM variable) and site number (SITEID variable), e.g, "DermEffects (Site 103)".*

Table 14.2.1.3.13
Cohort 1: Summary of Investigator Global Assessment (IGA) Success (Score of "Clear" or "Almost Clear" plus ≥2-point Improvement from Baseline) by Study Visit – Observed Data
Categorical Results
All Treated Population

Study Visit Category/Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Week 2	XX
IGA Success [1]	
Yes	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)
No	XX (XX.X%)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the All Treated population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.1

Table 14.2.1.4.1
Cohort 2: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Multiple Imputation
Categorical Results
ITT Population

	Cohort 2			
Study Visit Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX	XX
IGA ≥2-point Improvement from Baseline [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score with a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.4.2
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Multiple Imputation
Categorical Results
ITT Population

(Same shell as Table 14.2.1.3.2 but using the same first column as Table 14.2.1.4.1; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: The success scores were summarized using observed dataset. The odds ratio and P values were summarized using multiple imputation dataset. Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score with a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.4.3
Cohort 2: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.4.1; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score with a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.4.4
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data
Categorical Results
ITT Population

(Same shell as Table 14.2.1.4.2; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score with a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.1

Table 14.2.1.4.5
Cohort 1: Summary of Investigator Global Assessment (IGA) ≥2-point Improvement from Baseline by Study Visit – Observed Data
Categorical Results
All Treated Population

(Same shell as Table 14.2.1.3.13 but using the same first column as Table 14.2.1.4.1; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the All Treated population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] IGA ≥2-point Improvement from Baseline ("Yes") is defined as an IGA score with a ≥2-grade improvement from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.1

Table 14.2.1.5.1
Cohort 2: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation
ITT Population

	Cohort 2			
	ARQ-252 Cream 0.3% QD (N=XX)		ARQ-252 Cream 0.3% BID (N=XX)	
Study Visit Statistic	Observed	Change	Observed	Change
Baseline				
n	XX		XX	
Mean (SD)	XX.X (X.XX)		XX.X (X.XX)	
Median	XX.X		XX.X	
Min, Max	XX, XX		XX, XX	
Q1, Q3	XX.X		XX.X	
Week 2				
n	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X
Week 4				
n	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drugs (ARQ-252 Cream 0.1% QD, Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 8, 12, and 13.

Abbreviations: BID = twice daily; IGA = investigator global assessment; QD = once daily; SD = standard deviation.
Note: Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Subjects are summarized by averaging results over all imputed datasets within a subject before summarizing by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.6.1

Table 14.2.1.5.2
Cohort 2, Pooled Treatments: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation
ITT Population

	Cohort 2			
	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)		ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	
Study Visit Statistic	Observed	Change	Observed	Change
Baseline				
n	XX		XX	
Mean (SD)	XX.X (X.XX)		XX.X (X.XX)	
Median	XX.X		XX.X	
Min, Max	XX, XX		XX, XX	
Q1, Q3	XX.X		XX.X	
Week 2				
n	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X
Week 4				
n	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drug (Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 8, 12, and 13.

Abbreviations: IGA = investigator global assessment; SD = standard deviation.
Note: Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Subjects are summarized by averaging results over all imputed datasets within a subject before summarizing by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.6.1

Table 14.2.1.5.3
Cohort 2: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
ITT Population

(Same shell as Table 14.2.1.5.1; use the below footnotes)

Abbreviations: BID = twice daily; IGA = investigator global assessment; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.6.1

Table 14.2.1.5.4
Cohort 2, Pooled Treatments: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
ITT Population

(Same shell as Table 14.2.1.5.2; use the below footnotes)

Abbreviations: IGA = investigator global assessment; SD = standard deviation.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.6.1

Table 14.2.1.5.5
Cohort 1: Summary and Change from Baseline in Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data
All Treated Population

Study Visit / Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX) Observed	Change
Baseline		
n	XX	
Mean (SD)	XX.X (X.XX)	
Median	XX.X	
Min, Max	XX, XX	
Q1, Q3	XX.X	
Week 2		
n	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X

Abbreviations: IGA = investigator global assessment; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.6.1

Table 14.2.1.6.1
Cohort 2: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation – ANCOVA
ITT Population

Study Visit Category Statistic [1]	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2				
Change from Baseline				
n	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
(90% CI for Difference from Vehicle)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
(95% CI for Difference from Vehicle)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, and baseline IGA grade as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.1

Table 14.2.1.6.2
Cohort 2, Pooled Treatments: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Multiple Imputation – ANCOVA
ITT Population

Study Visit Category Statistic [1]	Cohort 2 ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	 ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2			
Change from Baseline			
n	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	X.XX (X.XXX)	X.XX (X.XXX)	
(90% CI for Difference from Vehicle)	(X.XX, X.XX)	(X.XX, X.XX)	
(95% CI for Difference from Vehicle)	(X.XX, X.XX)	(X.XX, X.XX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13.

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; SE = standard error.
Note: Separate multiple imputation steps were used for monotone and non-monotone missing data. For monotone missing pattern, a predictive mean matching model was used to impute missing value for a subject at particular visit having IGA score at previous study visit, treatment group, and pooled site group as independent variables and outcome at study visit as dependent variable. For non-monotone missing IGA values, Markov-Chain Monte Carlo (MCMC) method was used to impute the data at intermediate visits to make the missing data pattern into monotone before applying the predictive mean matching multiple imputation algorithm. Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, and baseline IGA grade as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.1

Table 14.2.1.6.3
Cohort 2: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
ITT Population

(Same shell as Table 14.2.1.6.1; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, and baseline IGA grade as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.1

Table 14.2.1.6.4
Cohort 2, Pooled Treatment: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
ITT Population

(Same shell as Table 14.2.1.6.2; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; SE = standard error.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, and baseline IGA grade as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.1

Table 14.2.1.6.5
Cohort 1: Summary of Investigator Global Assessment (IGA) Grades by Study Visit – Observed Data – ANCOVA
All Treated Population

Study Visit Category Statistic [1]	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Week 2	
Change from Baseline	
n	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. IGA is a static qualitative evaluation of overall chronic hand eczema severity involving an ordinal scale with 5 severity grades (reported only in integers of 0 to 4) where 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe.
[1] Estimates for LS means (change from baseline), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, and baseline IGA grade as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
Reference Listing: 16.2.6.1

Table 14.2.2.1.1
Cohort 2: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week
ITT Population

	Cohort 2					
	ARQ-252 Cream 0.3% QD (N=XX)			ARQ-252 Cream 0.3% BID (N=XX)		
Study Week Statistic	Observed	Change	% Change	Observed	Change	% Change
Baseline						
n	XX			XX		
Mean (SD)	XX.X (X.XX)			XX.X (X.XX)		
Median	XX.X			XX.X		
Min, Max	XX, XX			XX, XX		
Q1, Q3	XX.X			XX.X		
Week 1						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Week 2						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drugs (ARQ-252 Cream 0.1% QD, and Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.

Abbreviations: BID = twice daily; QD = once daily; SD = standard deviation; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by planned treatment. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.2

Table 14.2.2.1.2
Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week
ITT Population

	Cohort 2					
	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)			ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)		
Study Week Statistic	Observed	Change	% Change	Observed	Change	% Change
Baseline						
n	XX			XX		
Mean (SD)	XX.X (X.XX)			XX.X (X.XX)		
Median	XX.X			XX.X		
Min, Max	XX, XX			XX, XX		
Q1, Q3	XX.X			XX.X		
Week 1						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Week 2						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drug (Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.

Abbreviations: SD = standard deviation; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by planned treatment. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.2

Table 14.2.2.1.3
Cohort 2: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week – ANCOVA
ITT Population

Study Week Category Statistic [1]	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 1				
Change from Baseline				
n	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	X.XXXX	
Percent Change from Baseline				
n	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	X.XXXX	
Continue for Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.				

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by planned treatment. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline WI-NRS pruritus score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.2

Table 14.2.2.1.4
Cohort 2, Pooled Treatments: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week – ANCOVA
ITT Population

Study Week Category Statistic [1]	Cohort 2 ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	 ARQ-252 Cream (All Dose Frequencies) (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 1			
Change from Baseline			
n	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	
Percent Change from Baseline			
n	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	
Continue for Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.			

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by planned treatment. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline WI-NRS pruritus score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.2

Table 14.2.2.1.5
Cohort 2: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week – ANCOVA
PP Population

(Same shell as Table 14.2.2.1.3; visits include Baseline, Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, Week 8, Week 9, Week 10, Week 11, Week 12, and Week 13; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by treatment received. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline WI-NRS pruritus score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.2

Table 14.2.2.1.6
Cohort 2, Pooled Treatments: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week – ANCOVA
PP Population

(Same shell as Table 14.2.2.2.4; visits include Baseline, Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, Week 8, Week 9, Week 10, Week 11, Week 12, and Week 13; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; SE = standard error; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by treatment received. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline WI-NRS pruritus score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.2

Table 14.2.2.1.7
Cohort 2: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Week
ITT Population, Subjects with WI-NRS Pruritus Score ≥4 at Baseline (PRU4 Population)

	Cohort 2			
Study Week Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 1	XX	XX	XX	XX
WI-NRS ≥4-point Reduction from Baseline [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	
Continue for Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.				

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the PRU4 population within planned treatment at each visit*100. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] WI-NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly WI-NRS pruritus score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.2

Table 14.2.2.1.8
Cohort 2, Pooled Treatments: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Week
ITT Population, Subjects with WI-NRS Pruritus Score ≥4 at Baseline (PRU4 Population)

	Cohort 2		
Study Week Category/Statistic	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 1	XX	XX	XX
WI-NRS ≥4-point Reduction from Baseline [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	

Continue for Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13.

Abbreviations: CI = confidence interval; IGA = investigator global assessment; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the PRU4 population within planned treatment at each visit*100. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] WI-NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly WI-NRS pruritus score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.2

Table 14.2.2.1.9
Cohort 1: Summary and Change and Percent Change from Baseline in Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week
All Treated Population

Study Week Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX) Observed	Change	% Change
Baseline			
n	XX		
Mean (SD)	XX.X (X.XX)		
Median	XX.X		
Min, Max	XX, XX		
Q1, Q3	XX.X		
Week 1			
n	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X
Repeat for Week 2.			

Abbreviations: QD = once daily; SD = standard deviation; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by treatment received. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.2

Table 14.2.2.1.10
Cohort 1: Summary of Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Week – ANCOVA
All Treated Population

Study Week Category Statistic [1]	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Week 1	
Change from Baseline	
n	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX
Percent Change from Baseline	
n	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX
Repeat for Week 2.	

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Subjects are summarized by treatment received. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch".
[1] Estimates for LS means (change from baseline), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline WI-NRS pruritus score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
Reference Listing: 16.2.6.2

Table 14.2.2.1.11
Cohort 1: Average Weekly Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score Success (≥4-point Reduction from Baseline) by Study Week
All Treated Population, Subjects with WI-NRS Pruritus Score ≥4 at Baseline (PRU4 Population)

Study Week Category/Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Week 1	XX
WI-NRS ≥4-point Reduction from Baseline [1]	
Yes	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)
No	XX (XX.X%)
Week 2	XX
WI-NRS ≥4-point Reduction from Baseline [1]	
Yes	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)
No	XX (XX.X%)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Percentages are n/Number of subjects in the PRU4 population within treatment received at each visit*100. The WI-NRS pruritus score was determined by asking the subject's assessment of worst itch over the past 24 hours; average weekly WI-NRS pruritus scores were calculated as the average of the reported (non-missing) WI-NRS pruritus daily diary scores for each study week. The scale is from 0 to 10, which ranges from "no itch" to "worst imaginable itch". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] WI-NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly WI-NRS pruritus score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.2

Table 14.2.2.2.1
Cohort 2: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit
ITT Population

Parameter: Fingertips Subscore

	Cohort 2					
	ARQ-252 Cream 0.3% QD (N=XX)			ARQ-252 Cream 0.3% BID (N=XX)		
Study Visit Statistic	Observed	Change	% Change	Observed	Change	% Change
Baseline						
n	XX			XX		
Mean (SD)	XX.X (X.XX)			XX.X (X.XX)		
Median	XX.X			XX.X		
Min, Max	XX, XX			XX, XX		
Q1, Q3	XX.X			XX.X		
Week 2						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Week 4						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drugs (ARQ-252 Cream 0.1% QD, and Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 8, 12, and 13. Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.3

Table 14.2.2.2.2
Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit
ITT Population

Parameter: Fingertips Subscore

	Cohort 2					
	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)			ARQ-252 Cream (All Dose Frequencies) (N=XX)		
Study Visit Statistic	Observed	Change	% Change	Observed	Change	% Change
Baseline						
n	XX			XX		
Mean (SD)	XX.X (X.XX)			XX.X (X.XX)		
Median	XX.X			XX.X		
Min, Max	XX, XX			XX, XX		
Q1, Q3	XX.X			XX.X		
Week 2						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Week 4						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drug (Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 8, 12, and 13. Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.

Abbreviations: BID = twice daily; HECSI = Hand Eczema Severity Index; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.3

Table 14.2.2.2.3
Cohort 2: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
ITT Population

Parameter: Fingertips Subscore

Study Visit Category Statistic [1]	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2				
Change from Baseline				
n	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	X.XXXX	
Percent Change from Baseline				
n	XX	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13. Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline HECSI subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.3

Table 14.2.2.2.4
Cohort 2, Pooled Treatments: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
ITT Population

Parameter: Fingertips Subscore

	Cohort 2		
Study Visit Category Statistic [1]	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	ARQ-252 Cream (All Dose Frequencies) (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2			
Change from Baseline			
n	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	
Percent Change from Baseline			
n	XX	XX	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)	X.XX (X.XXX)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX	X.XXXX	X.XXXX
LS Mean Difference from Vehicle (SE)	(X.XX, X.XX)	(X.XX, X.XX)	
(90% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
(95% CI for Difference from Vehicle)	X.XX (X.XXX)	X.XX (X.XXX)	
P value for Difference from Vehicle [3]	X.XXXX	X.XXXX	

Continue for Weeks 4, 8, 12, and 13. Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; LS = least-squares; SE = standard error.
Note: Subjects are summarized by planned treatment. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline HECSI subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.3

Table 14.2.2.2.5

Cohort 2: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
PP Population

(Same shell as Table 14.2.2.2.3; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by treatment received. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline HECSI subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.3

Table 14.2.2.2.6
Cohort 2, Pooled Treatments: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
PP Population

(Same shell as Table 14.2.2.2.4; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by treatment received. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline HECSI subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.3

Table 14.2.2.2.7
Cohort 2: Summary of Achievement of HECSI-75 by Study Visit
ITT Population

	Cohort 2			
Study Visit Category/Statistic	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX	XX
HECSI-75 [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	
Week 4	XX	XX	XX	XX
HECSI-75 [1]				
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	X.XXXX	

Continue for Weeks 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the first application of study drug.
[1] HECSI-75 is populated with "Yes" when there is an achievement of a 75% reduction in HECSI total score from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.3

Table 14.2.2.2.8
Cohort 2, Pooled Treatments: Summary of Achievement of HECSI-75 by Study Visit
ITT Population

Study Visit Category/Statistic	Cohort 2 ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)	Cohort 2 ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)	Cohort 2 Vehicle Cream (All Dose Frequencies) (N=XX)
Week 2	XX	XX	XX
HECSI-75 [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	
Week 4	XX	XX	XX
HECSI-75 [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
90% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
95% CI [2]	(X.XX, X.XX)	(X.XX, X.XX)	(X.XX, X.XX)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Odds Ratio (90% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
P value [3]	X.XXXX	X.XXXX	

Continue for Weeks 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; QD = once daily.
Note: Percentages are n/Number of subjects in the ITT population within planned treatment at each visit*100. Baseline is the last non-missing measurement taken on or before the first application of study drug.
[1] HECSI-75 is populated with "Yes" when there is an achievement of a 75% reduction in HECSI total score from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.3

Table 14.2.2.2.9
Cohort 2: Summary of Achievement of HECSI-75 by Study Visit
PP Population

(Same shell as Table 14.2.2.2.7; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; QD = once daily.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the first application of study drug.
[1] HECSI-75 is populated with "Yes" when there is an achievement of a 75% reduction in HECSI total score from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.3

Table 14.2.2.2.10
Cohort 2, Pooled Treatments: Summary of Achievement of HECSI-75 by Study Visit
PP Population

(Same shell as Table 14.2.2.2.8; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; HECSI = Hand Eczema Severity Index; QD = once daily.
Note: Percentages are n/Number of subjects in the PP population within treatment received at each visit*100. Baseline is the last non-missing measurement taken on or before the first application of study drug.
[1] HECSI-75 is populated with "Yes" when there is an achievement of a 75% reduction in HECSI total score from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.3

Table 14.2.2.2.11
Cohort 1: Summary and Change and Percent Change from Baseline in Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit
All Treated Population

Parameter: Fingertips Subscore

Study Visit / Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)		
	Observed	Change	% Change
Baseline			
n	XX		
Mean (SD)	XX.X (X.XX)		
Median	XX.X		
Min, Max	XX, XX		
Q1, Q3	XX.X		
Week 2			
n	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X

Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.

Abbreviations: HECSI = Hand Eczema Severity Index; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.3

Table 14.2.2.2.12
Cohort 1: Summary of Hand Eczema Severity Index (HECSI) Subscores and Total Score by Study Visit – ANCOVA
All Treated Population

Parameter: Fingertips Subscore Study Visit Category Statistic [1]	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Week 2	
Change from Baseline	
n	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX
Percent Change from Baseline	
n	XX
LS Mean Change from Baseline (SE)	X.XX (X.XXX)
(90% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
(95% CI for LS Mean Change from Baseline)	(X.XX, X.XX)
P value for LS Mean Change from Baseline [2]	X.XXXX
Repeat everything for the following parameters: Fingers (except Tips) Subscore, Palm of Hands Subscore, Back of Hands Subscore, Wrists Subscore, and Total Score.	

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by treatment received. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The range for each subscore is 0 to 72, and the range for the total score is 0 to 360. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline HECSI subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
Reference Listing: 16.2.6.3

Table 14.2.2.3.1
Cohort 2: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week
ITT Population

(Same shell as Table 14.2.2.1.1; use the below footnotes)

Abbreviations: BID = twice daily; NRS = Numeric Rating Scale; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.4

Table 14.2.2.3.2
Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week
ITT Population

(Same shell as Table 14.2.2.1.2; use the below footnotes)

Abbreviations: NRS = Numeric Rating Scale; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.4

Table 14.2.2.3.3
Cohort 2: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week – ANCOVA
ITT Population

(Same shell as Table 14.2.2.1.3; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; NRS = Numeric Rating Scale; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline Pain NRS score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.4

Table 14.2.2.3.4
Cohort 2, Pooled Treatments: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week – ANCOVA
ITT Population

(Same shell as Table 14.2.2.1.4; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; NRS = Numeric Rating Scale; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline Pain NRS score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.4

Table 14.2.2.3.5
Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥4 at Baseline (PNRS4 Population)

(Same shell as Table 14.2.2.1.7; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS4 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.6
Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥4 at Baseline (PNRS4 Population)

(Same shell as Table 14.2.2.1.8; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS4 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.7
Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥3 at Baseline (PNRS3 Population)

(Same shell as Table 14.2.2.1.7; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS3 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥3-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥3-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.8
Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥3 at Baseline (PNRS3 Population)

(Same shell as Table 14.2.2.1.8; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS3 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥3-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥3-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.9
Cohort 2: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥2 at Baseline (PNRS2 Population)

(Same shell as Table 14.2.2.1.7; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS2 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥2-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥2-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream 0.3% QD vs vehicle cream (all dose frequencies); ARQ-252 cream 0.3% BID vs vehicle cream (all dose frequencies); and ARQ-252 cream 0.1% QD vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.10
Cohort 2, Pooled Treatments: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Week
ITT Population, Subjects with Pain NRS Score ≥2 at Baseline (PNRS2 Population)

(Same shell as Table 14.2.2.1.8; change instances of "WI-NRS" in table to "Pain NRS"; use the below footnotes)

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS2 population within planned treatment at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥2-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥2-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
[3] The odds ratio, 90% and 95% CIs, and P value are obtained from Cochran Mantel Haenszel test (stratified by pooled site group and baseline IGA grade) comparing: ARQ-252 cream (all strengths/dose frequencies) vs vehicle cream (all dose frequencies) and ARQ-252 cream 0.3% (all dose frequencies) vs vehicle cream (all dose frequencies).
Reference Listing: 16.2.6.4

Table 14.2.2.3.11
Cohort 1: Summary and Change and Percent Change from Baseline in Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week
All Treated Population

(Same shell as Table 14.2.2.1.9; visits include Baseline, Week 1, and Week 2; use the below footnotes)

Abbreviations: NRS = Numeric Rating Scale; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.4

Table 14.2.2.3.12
Cohort 1: Summary of Average Weekly Pain Numeric Rating Scale (NRS) Score by Study Week – ANCOVA
All Treated Population

(Same shell as Table 14.2.2.1.10; visits include Baseline, Week 1, and Week 2; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; NRS = Numeric Rating Scale; QD = once daily; SE = standard error.
Note: Subjects are summarized by treatment received. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain".
[1] Estimates for LS means (change from baseline), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline Pain NRS score as independent variables. Baseline is the last non-missing measurement taken before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
Reference Listing: 16.2.6.4

Table 14.2.2.3.13
Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥4-point Reduction from Baseline) by Study Week
All Treated Population, Subjects with Pain NRS Score ≥4 at Baseline (PNRS4 Population)

(Same shell as Table 14.2.2.1.11; visits include Baseline, Week 1, and Week 2; replace instances of WI-NRS with Pain NRS; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS4 population within treatment received at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥4-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥4-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.4

Table 14.2.2.3.14
Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥3-point Reduction from Baseline) by Study Week
All Treated Population, Subjects with Pain NRS Score ≥3 at Baseline (PNRS3 Population)

(Same shell as Table 14.2.2.1.11; visits include Baseline, Week 1, and Week 2; replace instances of WI-NRS with Pain NRS; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS3 population within treatment received at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥3-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥3-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.4

Table 14.2.2.3.15
Cohort 1: Average Weekly Pain Numeric Rating Scale (NRS) Score Success (≥2-point Reduction from Baseline) by Study Week
All Treated Population, Subjects with Pain NRS Score ≥2 at Baseline (PNRS2 Population)

(Same shell as Table 14.2.2.1.11; visits include Baseline, Week 1, and Week 2; replace instances of WI-NRS with Pain NRS; use the below footnotes)

Abbreviations: CI = confidence interval; IGA = investigator global assessment; NRS = Numeric Rating Scale; QD = once daily.
Note: Percentages are n/Number of subjects in the PNRS2 population within treatment received at each visit*100. The Pain NRS is the subject's assessment of worst pain intensity over the past 24 hours; average weekly Pain NRS scores were calculated as the average of the reported (non-missing) Pain NRS daily diary scores for each study week. The scale is from 0 to 10, which ranges from 0 = "no pain" and 10 = "worst possible pain". Baseline is the last non-missing measurement taken before the day of first application of study drug.
[1] Pain NRS ≥2-point Reduction from Baseline ("Yes") is defined as an average weekly Pain NRS score with a ≥2-point reduction from baseline; "No" otherwise.
[2] 90% and 95% CIs for "Yes" are obtained using Wilson method.
Reference Listing: 16.2.6.4

Table 14.2.2.4.1
Cohort 2: Summary and Change and Percent Change from Baseline in Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit
ITT Population

(Same shell as Table 14.2.2.2.1; parameters include the following: Symptoms Subscore, Emotions Subscore, Limitations in Functioning Subscore, Treatment and Prevention Subscore, and Total Score; use the below footnotes)

Abbreviations: BID = twice daily; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The construct Health Related Quality of Life (HRQOL) includes all impairments or limiting conditions caused by the health state of an individual. The QOLHEQ is a disease specific instrument, thereby only assessing impairments caused by hand eczema. It consists of 30 items which can be summarized according to these four domains: Impairments because of (1) symptoms (range 0 to 27), (2) emotions (range 0 to 31), (3) limitations in functioning (range 0 to 32), or (4) because of treatment and prevention (range 0 to 27); the total score is the sum of the subscores and has a range of 0 to 117. Lower scores indicate better outcomes. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.5

Table 14.2.2.4.2
Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit
ITT Population

(Same shell as Table 14.2.2.2.2; parameters include the following: Symptoms Subscore, Emotions Subscore, Limitations in Functioning Subscore, Treatment and Prevention Subscore, and Total Score; use the below footnotes)

Abbreviations: QOLHEQ = Quality of Life in Hand Eczema Questionnaire; SD = standard deviation.
Note: Subjects are summarized by planned treatment. The construct Health Related Quality of Life (HRQOL) includes all impairments or limiting conditions caused by the health state of an individual. The QOLHEQ is a disease specific instrument, thereby only assessing impairments caused by hand eczema. It consists of 30 items which can be summarized according to these four domains: Impairments because of (1) symptoms (range 0 to 27), (2) emotions (range 0 to 31), (3) limitations in functioning (range 0 to 32), or (4) because of treatment and prevention (range 0 to 27); the total score is the sum of the subscores and has a range of 0 to 117. Lower scores indicate better outcomes. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.5

Table 14.2.2.4.3
Cohort 2: Summary of Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit – ANCOVA
ITT Population

(Same shell as Table 14.2.2.2.3; parameters include the following: Symptoms Subscore, Emotions Subscore, Limitations in Functioning Subscore, Treatment and Prevention Subscore, and Total Score; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; SE = standard error.
Note: Subjects are summarized by planned treatment. The construct Health Related Quality of Life (HRQOL) includes all impairments or limiting conditions caused by the health state of an individual. The QOLHEQ is a disease specific instrument, thereby only assessing impairments caused by hand eczema. It consists of 30 items which can be summarized according to these four domains: Impairments because of (1) symptoms (range 0 to 27), (2) emotions (range 0 to 31), (3) limitations in functioning (range 0 to 32), or (4) because of treatment and prevention (range 0 to 27); the total score is the sum of the subscores and has a range of 0 to 117. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline QOLHEQ subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.5

Table 14.2.2.4.4
Cohort 2, Pooled Treatments: Summary of Quality of Life in Hand Eczema Questionnaire (QOLHEQ) Subscores and Total Score by Study Visit – ANCOVA
ITT Population

(Same shell as Table 14.2.2.2.4; parameters include the following: Symptoms Subscore, Emotions Subscore, Limitations in Functioning Subscore, Treatment and Prevention Subscore, and Total Score; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; SE = standard error.
Note: Subjects are summarized by planned treatment. The construct Health Related Quality of Life (HRQOL) includes all impairments or limiting conditions caused by the health state of an individual. The QOLHEQ is a disease specific instrument, thereby only assessing impairments caused by hand eczema. It consists of 30 items which can be summarized according to these four domains: Impairments because of (1) symptoms (range 0 to 27), (2) emotions (range 0 to 31), (3) limitations in functioning (range 0 to 32), or (4) because of treatment and prevention (range 0 to 27); the total score is the sum of the subscores and has a range of 0 to 117. Lower scores indicate better outcomes.
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline QOLHEQ subscore or total score (as appropriate) as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.5

Table 14.2.2.5.1
Cohort 2: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
ITT Population

(Same shell as Table 14.2.2.2.1; parameters include "Dorsal BSA (Left Hand)", "Dorsal BSA (Right Hand)", "Palmar BSA (Left Hand)", "Palmar BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: BID = twice daily; BSA = body surface area; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by planned treatment. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand). Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.6

Table 14.2.2.5.2
Cohort 2, Pooled Treatments: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
ITT Population

(Same shell as Table 14.2.2.2.2; parameters include "Dorsal BSA (Left Hand)", "Dorsal BSA (Right Hand)", "Palmar BSA (Left Hand)", "Palmar BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: BSA = body surface area; SD = standard deviation.
Note: Subjects are summarized by planned treatment. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand). Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.6

Table 14.2.2.5.3
Cohort 2: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA
ITT Population

(Same shell as Table 14.2.2.2.3; parameters include "Dorsal % BSA (Left Hand)", "Dorsal % BSA (Right Hand)", "Palmar % BSA (Left Hand)", "Palmar % BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BID = twice daily; BSA = body surface area; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand).
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline % BSA affected by disease as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream 0.3% QD minus vehicle cream [all dose frequencies]; ARQ-252 cream 0.3% BID minus vehicle cream [all dose frequencies]; or ARQ-252 cream 0.1% QD minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.6

Table 14.2.2.5.4
Cohort 2, Pooled Treatments: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA
ITT Population

(Same shell as Table 14.2.2.2.4; parameters include "Dorsal % BSA (Left Hand)", "Dorsal % BSA (Right Hand)", "Palmar % BSA (Left Hand)", "Palmar % BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BSA = body surface area; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; SE = standard error.
Note: Subjects are summarized by planned treatment. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand).
[1] Estimates for LS means (change from baseline and difference from vehicle), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline % BSA affected by disease as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
[3] P value for testing difference (ARQ-252 cream [all strengths/dose frequencies] minus vehicle cream [all dose frequencies] or ARQ-252 cream 0.3% [all dose frequencies] minus vehicle cream [all dose frequencies]) in change from baseline from is zero.
Reference Listing: 16.2.6.6

Table 14.2.2.5.5
Cohort 1: Summary and Change and Percent Change from Baseline in % Body Surface Area (BSA) Affected by Disease by Study Visit
All Treated Population

(Same shell as Table 14.2.2.2.11; visits include Baseline and Week 2; parameters include "Dorsal % BSA (Left Hand)", "Dorsal % BSA (Right Hand)", "Palmar % BSA (Left Hand)", "Palmar % BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: BSA = body surface area; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand). Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
Reference Listing: 16.2.6.6

Table 14.2.2.5.6
Cohort 1: Summary of % Body Surface Area (BSA) Affected by Disease by Study Visit – ANCOVA
All Treated Population

(Same shell as Table 14.2.2.2.11; visits include Baseline and Week 2; parameters include "Dorsal % BSA (Left Hand)", "Dorsal % BSA (Right Hand)", "Palmar % BSA (Left Hand)", "Palmar % BSA (Right Hand)", and "Total Hand % BSA"; use the below footnotes)

Abbreviations: ANCOVA = analysis of covariance; BSA = body surface area; CI = confidence interval; IGA = investigator global assessment; LS = least-squares; QD = once daily; SE = standard error.
Note: Subjects are summarized by planned treatment. Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand).
[1] Estimates for LS means (change from baseline), accompanying 90% and 95% CIs, and P values are from an ANCOVA with treatment group, pooled site group, baseline IGA grade, and baseline % BSA affected by disease as independent variables. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[2] P value for testing change from baseline is zero.
Reference Listing: 16.2.6.6

Table 14.2.3.1
Cohort 2: Summary of Nail Dystrophy Normal-Appearing Nail Distal to Cuticle (mm) by Study Visit
Nail Dystrophy Population

	Cohort 2					
	ARQ-252 Cream 0.3% QD (N=XX)		ARQ-252 Cream 0.3% BID (N=XX)		ARQ-252 Cream 0.1% QD (N=XX)	
Study Visit Category/Statistic	Observed	Change	Observed	Change	Observed	Change
Baseline	XX		XX		XX	
Nail with Worst Dystrophy						
Left	XX (XX.X%)		XX (XX.X%)		XX (XX.X%)	
Right	XX (XX.X%)		XX (XX.X%)		XX (XX.X%)	
Week 2	XX		XX		XX	
Normal Appearing Nail Distal to Cuticle?						
Yes	XX (XX.X%)		XX (XX.X%)		XX (XX.X%)	
No	XX (XX.X%)		XX (XX.X%)		XX (XX.X%)	
Normal Appearing Nail Distal to Cuticle (mm) [1]						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat this page for the remaining study drug (Vehicle Cream (All Dose Frequencies)), showing the same study visits shown here. Then continue for Weeks 4, 8, 12, and 13.

Abbreviations: BID = twice daily; CI = confidence interval; IGA = investigator global assessment; QD = once daily.
Note: Percentages are n/Number of subjects in the Nail Dystrophy population within planned treatment at each visit*100. Only subjects with nail dystrophy at baseline are included in this table. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] Relative to an assumed baseline normal appearing nail distal to cuticle value of 0 mm.
Reference Listing: 16.2.6.7

Table 14.2.3.2
Cohort 2, Pooled Treatments: Summary of Nail Dystrophy Normal-Appearing Nail Distal to Cuticle (mm) by Study Visit
Nail Dystrophy Population

	Cohort 2					
	ARQ-252 Cream (All Strengths/Dose Frequencies) (N=XX)		ARQ-252 Cream 0.3% (All Dose Frequencies) (N=XX)		Vehicle Cream (All Dose Frequencies) (N=XX)	
Study Visit Category/Statistic	Observed	Change	Observed	Change	Observed	Change
Baseline	XX	XX	XX	XX	XX	XX
Nail with Worst Dystrophy						
Left	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Right	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2	XX	XX	XX	XX	XX	XX
Normal Appearing Nail Distal to Cuticle?						
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Normal Appearing Nail Distal to Cuticle (mm) [1]						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Q1, Q3	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

Repeat for Weeks 4, 8, 12, and 13.

Abbreviations: CI = confidence interval; IGA = investigator global assessment.
Note: Percentages are n/Number of subjects in the Nail Dystrophy population within planned treatment at each visit*100. Only subjects with nail dystrophy at baseline are included in this table. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
[1] Relative to an assumed baseline normal appearing nail distal to cuticle value of 0 mm.
Reference Listing: 16.2.6.7

Table 14.3.1.1
Cohorts 1 and 2: Summary of Treatment Emergent Adverse Events
Safety Population

Category	Cohort 1	Cohort 2				
	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Subjects with at least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Maximum Severity of TEAE [1]						
Grade 1 (Mild)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 2 (Moderate)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 3 (Severe)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 4 (Life-threatening consequences)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 5 (Death related to AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a Related TEAE [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a Related TEAE Leading to Discontinuation of Study Drug [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a TEAE Leading to Discontinuation of Study Drug	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a TEAE Leading to Discontinuation of Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with an SAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a Grade 5 TEAE [3]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; QD = once daily; SAE = serious adverse event; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion.
[1] Severity grades are reported according to the CTCAE version 4.0. Subjects are counted only once at the worst severity. If a severity designation is missing, it was considered as severe.
[2] AEs with a relationship of possibly related, probably related, likely related, or missing were considered related.
[3] A Grade 5 TEAE is a TEAE leading to death.
Reference Listing: 16.2.7.1

Table 14.3.1.2
Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Subjects with at least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; QD = once daily; SAE = serious adverse event; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. AEs were coded using MedDRA version 23.0. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. Subjects are counted once for each SOC and once for each PT. AEs are displayed alphabetically by SOC, then by descending frequency of PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming note: *SOC & PT text should be presented as is from the dataset.*

Table 14.3.1.3
Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population

System Organ Class Preferred Term Maximum Severity [1]	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Subjects with at least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 1 (Mild)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 2 (Moderate)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 3 (Severe)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 4 (Life-threatening consequences)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 5 (Death related to AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 1 (Mild)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 2 (Moderate)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 3 (Severe)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 4 (Life-threatening consequences)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 5 (Death related to AE)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 1 (Mild)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Grade 2 (Moderate)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…						

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; QD = once daily; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. AEs were coded using MedDRA version 23.0. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. Subjects are counted once for each SOC and once for each PT.
[1] Severity grades are reported according to the CTCAE version 4.0. The severity shown is the greatest severity reported for a particular subject (Grade 5 [Death related to AE] > Grade 4 [Life-threatening consequences] > Grade 3 [Severe] > Grade 2 [Moderate] > Grade 1 [Mild]). AEs with a missing severity were counted as Severe. AEs are displayed alphabetically by SOC, then by descending frequency of PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming note: *SOC & PT text should be presented as is from the dataset.*

Table 14.3.1.4
Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug
Safety Population

	Cohort 1	Cohort 2				
System Organ Class Preferred Term Relationship [1]	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Subjects with at least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…						

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; QD = once daily; SAE = serious adverse event; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. AEs were coded using MedDRA version 23.0. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. Subjects are counted once for each SOC and once for each PT at the greatest relationship category. The relationship shown is the greatest relationship reported for a particular subject (Related > Not Related). AEs with a missing relationship were counted as Related. AEs are displayed alphabetically by SOC, then by descending frequency of PT within SOC, and then alphabetically by PT.
[1] Related = Probably Related, Possibly Related, Likely Related, and missing; Not Related = Unrelated and Unlikely Related.
Reference Listing: 16.2.7.1

Programming note: *SOC & PT text should be presented as is from the dataset.*

Table 14.3.1.5
Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term
Safety Population

(Same shell as Table 14.3.1.2)

Table 14.3.1.6
Cohorts 1 and 2: Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term
Safety Population

(Same shell as Table 14.3.1.2; use the below footnotes)

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; QD = once daily; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. AEs were coded using MedDRA version 23.0. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. Related TEAEs are AE marked Probably Related, Possibly Related, Likely Related, or missing. Subjects are counted once for each SOC and once for each PT. AEs are displayed alphabetically by SOC, then by descending frequency of PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Table 14.3.1.7
Cohorts 1 and 2: Incidence of Treatment Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term
Safety Population

(Same shell as Table 14.3.1.2)

Table 14.3.1.8
Cohorts 1 and 2: Incidence of Related Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population

(Same shell as Table 14.3.1.3; updated 1st line of the table to say, "Subjects with at least 1 Related TEAE"; use the below footnotes)

Abbreviations: AE = adverse event; BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; QD = once daily; SAE = serious adverse event; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. AEs were coded using MedDRA version 23.0. A TEAE is defined as an AE within an onset on or after the day of study treatment through study completion. Related TEAEs are AE marked Probably Related, Possibly Related, Likely Related, or missing. Subjects are counted once for each SOC and once for each PT.
[1] Severity grades are reported according to the CTCAE version 4.0. The severity shown is the greatest severity reported for a particular subject (Grade 5 [Death related to AE] > Grade 4 [Life-threatening consequences] > Grade 3 [Severe] > Grade 2 [Moderate] > Grade 1 [Mild]). AEs with a missing severity were counted as Severe. AEs are displayed alphabetically by SOC, then by descending frequency of PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Table 14.3.2.1
Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

(Same shell as Table 14.3.1.2; first-row text is "Subjects with at least 1 SAE**"; add** SAE = serious adverse event**)**

Table 14.3.2.2
Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population

(Same shell as Table 14.3.1.3; first-row text is "Subjects with at least 1 SAE**"; add** SAE = serious adverse event**)**

Table 14.3.2.3
Cohorts 1 and 2: Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug
Safety Population

(Same shell as Table 14.3.1.4; first-row text is "Subjects with at least 1 SAE**"; add** SAE = serious adverse event**)**

Table 14.3.3.1
Listing of Adverse Events Leading to Study Drug Discontinuation
Safety Population

Cohort: Cohort x

Subject ID	Treatment [1]	TEAE?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	CTCAE Toxicity Grade/ Relationship	Outcome/ Action Taken/ Other Action Taken	Serious?	AE Lead to Study D/C?
XXXXX	XXXXXX	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/hh:mm (X)/ DDMMMYYYY/ hh:mm (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XX	XX
XXXXX	XXXXXX	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/ hh:mm (X)/ DDMONYYYY/ hh:mm (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XX	XX
		XX	XXXXXXXXXXXXXX/ XXXXXXXXXXXX XXXXXXXXXXXXX	DDMONYYYY/ hh:mm (X)/ Ongoing	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XXX	XXX

Abbreviations: BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; D/C = discontinuation; MedDRA = Medical Dictionary for Regulatory Activities; QD = once daily; TEAE = treatment emergent adverse event.
Note: Study day is calculated relative to the date of first application of study drug. AEs were coded using MedDRA version 23.0. Severity grades are reported according to the CTCAE version 4.0. All AEs with an onset on or after the day of study treatment through study completion are considered as TEAEs.
[1] Treatment received for both cohorts.

Programming note: *If time missing, display "- -:- -". "Other Action Taken" will be either None, Concomitant Medication, Non-drug Therapy, Hospitalization or Prolongation of Hospitalization, Discontinued Study or Other; if specify text is needed, concatenate "Concomitant Medication:" or "Other:" with the text. If no events meet the criteria for display, present "No adverse events leading to study drug discontinuation were reported for this study." SOC & PT text should presented as is from the dataset.*

Table 14.3.3.2
Listing of Serious Adverse Events
Safety Population

(Same shell as Table 14.3.3.1; if no events meet the criteria for display, present "No serious adverse events were reported for this study.")

Table 14.3.3.3
Listing of Deaths
Safety Population

(Same shell as Table 14.3.3.1; if no events meet the criteria for display, present "No deaths were reported for this study.")

Table 14.3.5.1.1.1
Cohort 1: Summary of Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Safety Population

Parameter: XXXXXXXXXXXX (unit)

Study Visit Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX) Observed	 Change
Baseline		
n	XX	
Mean (SD)	XX.X (X.XX)	
Median	XX.X	
Min, Max	XX, XX	
Week 1		
n	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 2		
n	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 3		
n	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX

Continue for other parameters. Sort alphabetically by parameter.

Abbreviations: QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Results from the thyroid panel are included.
Baseline is the last non-missing measurement taken before the first application of study drug.
Change from baseline is calculated as result – baseline result.
Reference Listings: 16.2.8.1.1, 16.2.8.1.4

Table 14.3.5.1.1.2
Cohort 2: Summary of Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Safety Population

Parameter: XXXXXXXXXXXX (unit)

	Cohort 2					
	ARQ-252 Cream 0.3% QD (N=XX)		ARQ-252 Cream 0.3% BID (N=XX)		ARQ-252 Cream 0.1% QD (N=XX)	
Study Visit Statistic	Observed	Change	Observed	Change	Observed	Change
Baseline						
n	XX		XX		XX	
Mean (SD)	XX.X (X.XX)		XX.X (X.XX)		XX.X (X.XX)	
Median	XX.X		XX.X		XX.X	
Min, Max	XX, XX		XX, XX		XX, XX	
Week 4						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 8						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 12						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Repeat this page for the remaining study drugs (Vehicle Cream QD and Vehicle Cream BID), showing the same study visits shown here. Continue for other parameters. Sort alphabetically by parameter.

Abbreviations: BID = twice daily; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Results from the thyroid panel are included. Baseline is the last non-missing measurement taken before the first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listings: 16.2.8.1.1, 16.2.8.1.4

Table 14.3.5.1.2.1
Cohort 1: Shift from Baseline in Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Safety Population

Parameter: XXXXXXX (unit)

		Baseline Grade				
		Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)				
Study Visit	Post-Baseline Grade	Missing	Low	Normal	High	Total
Week 1	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 2	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 3	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Repeat all for clinical chemistry parameters (excluding serum HCG results).

Abbreviation: QD = once daily.
Note: Subjects are summarized by treatment received. Results from the thyroid panel are included. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listings: 16.2.8.1.1, 16.2.8.1.4

Table 14.3.5.1.2.2
Cohort 2: Shift from Baseline in Clinical Chemistry Laboratory Results (Standard Units) by Study Visit
Safety Population

Parameter: XXXXXXX (unit)

		Baseline Grade									
		Cohort 2									
	Post-Baseline	ARQ-252 Cream 0.3% QD (N=XX)					ARQ-252 Cream 0.3% BID (N=XX)				
Study Visit	Grade	Missing	Low	Normal	High	Total	Missing	Low	Normal	High	Total
Week 4	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 8	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 12	Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Repeat this page for the remaining study drugs (ARQ-252 Cream 0.1% QD, Vehicle Cream QD, and Vehicle Cream BID), showing the same study visits shown here. Repeat all for clinical chemistry parameters (excluding serum HCG results).

Abbreviations: BID = twice daily; QD = once daily.
Note: Subjects are summarized by treatment received. Results from the thyroid panel are included. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listings: 16.2.8.1.1, 16.2.8.1.4

Table 14.3.5.2.1.1
Cohort 1: Summary of Hematology Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.1; Reference Listing: 16.2.8.1.2)

Table 14.3.5.2.1.2
Cohort 2: Summary of Hematology Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.2; Reference Listing: 16.2.8.1.2)

Table 14.3.5.2.2.1
Cohort 1: Shift from Baseline in Hematology Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.2.1; Reference Listing: 16.2.8.1.2)

Table 14.3.5.2.2.2
Cohort 2: Shift from Baseline in Hematology Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.2.2; Reference Listing: 16.2.8.1.2)

Table 14.3.5.3.1.1
Cohort 1: Summary of Quantitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.1; Reference Listing: 16.2.8.1.3)

Table 14.3.5.3.1.2
Cohort 2: Summary of Quantitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.2; Reference Listing: 16.2.8.1.3)

Table 14.3.5.3.2.1
Cohort 1: Shift from Baseline in Quantitative and Qualitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.2.1; Reference Listing: 16.2.8.1.3)

Table 14.3.5.3.2.2
Cohort 2: Shift from Baseline in Quantitative and Qualitative Urinalysis Laboratory Results (Standard Units) by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.2.2; Reference Listing: 16.2.8.1.3)

Table 14.3.5.3.3.1
Cohort 1: Summary of Qualitative Urinalysis Laboratory Results by Study Visit
Safety Population

Parameter: XXXXXXXXXXXX (unit)

Study Visit Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Baseline	
XXXXXXXXXX	XX (XX.X%)
XXXXXXXXXXXX	XX (XX.X%)
Week 1	
XXXXXXXXX	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)
XXXXXXXX	XX (XX.X%)
Week 2	
XXXXXXXXX	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)
XXXXXXXX	XX (XX.X%)
Week 3	
XXXXXXXXX	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)
XXXXXXXX	XX (XX.X%)

Abbreviation: QD = once daily; TNTC = too numerous to count.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.8.1.3

Table 14.3.5.3.3.2
Cohort 2: Summary of Qualitative Urinalysis Laboratory Results by Study Visit
Safety Population

Parameter: XXXXXXXXXXXX (unit)

Study Visit Category	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Baseline					
XXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 4					
XXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 8					
XXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 12					
XXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; QD = once daily; TNTC = too numerous to count.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.8.1.3

Table 14.3.6.1.1
Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit
Safety Population

	Cohort 1		Cohort 2			
	ARQ-252 Cream 0.3% BID (N=XX)		ARQ-252 Cream 0.3% QD (N=XX)		ARQ-252 Cream 0.3% BID (N=XX)	
Study Visit Statistic	Observed	Change	Observed	Change	Observed	Change
Baseline						
n	XX		XX		XX	
Mean (SD)	XX.X (X.XX)		XX.X (X.XX)		XX.X (X.XX)	
Median	XX.X		XX.X		XX.X	
Min, Max	XX, XX		XX, XX		XX, XX	
Week 1						
n	XX	XX	NA	NA	NA	NA
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)				
Median	XX.X	XX.X				
Min, Max	XX, XX	XX, XX				
Week 2						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Repeat this page for the remaining Cohort 2 study drugs (ARQ-252 Cream 0.1% QD, Vehicle Cream QD, and Vehicle Cream BID), showing the same study visits shown here. Continue for the following study visits, applicable to Cohort 2 only: Week 4, Week 8, and Week 12; put "NA" in the "n" row for Cohort 1 for these visits.

Abbreviations: BID = twice daily; NA = not applicable; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. The Week 1 study visit is only applicable to Cohort 1 subjects; the Week 4 through Week 12 study visits are only applicable to Cohort 2 subjects. Lower scores indicate no evidence of irritation while higher scores indicate worsening reaction. These assessments should be done prior to the study drug application in the study site. Subjects not meeting this condition on baseline visit are completely removed from the table summary. Baseline is the last non-missing measurement taken before the first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.9.1

Table 14.3.6.1.2
Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit
Categorical Results
Safety Population

Study Visit Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)
Baseline	XX	XX	XX	XX	XX	XX
0 = No evidence of irritation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Minimal erythema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Definite erythema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Erythema and papules	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4 = Definite edema	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5 = Erythema, edema and papules	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6 = Vesicular eruption	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7 = Strong reaction spreading beyond application site	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 1	XX	NA	NA	NA	NA	NA
0 = No evidence of irritation	XX (XX.X%)					
1 = Minimal erythema	XX (XX.X%)					
2 = Definite erythema	XX (XX.X%)					
3 = Erythema and papules	XX (XX.X%)					
4 = Definite edema	XX (XX.X%)					
5 = Erythema, edema and papules	XX (XX.X%)					
6 = Vesicular eruption	XX (XX.X%)					
7 = Strong reaction spreading beyond application site	XX (XX.X%)					
Week 2	XX	XX	XX	XX	XX	XX
0 = No evidence of irritation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Continue for the following study visits, applicable to Cohort 2 only: Week 4, Week 8, and Week 12; put "NA" in the study visit row for Cohort 1 for these visits.

Abbreviations: BID = twice daily; NA = not applicable; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received, study visit, and overall*100. The Week 1 study visit is only applicable to Cohort 1 subjects; the Week 4 through Week 12 study visits are only applicable to Cohort 2 subjects. These assessments should be done prior to the study drug application in the study site. Subjects not meeting this condition on baseline visit are completely removed from the table summary. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.9.1

Table 14.3.6.1.3
Cohorts 1 and 2: Summary of Investigator Local Tolerability Assessment (Other Effects) by Study Visit
Categorical Results
Safety Population

Study Visit Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Baseline	XX	XX	XX	XX	XX	XX
A = Slight glazed appearance	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
B = Marked glazing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
C = Glazing with peeling and cracking	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
D = Glazing with fissures	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
E = Film of dried serous exudates	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
F = Small petechial erosions and/or scabs	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
G = No other effects	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 1	XX	NA	NA	NA	NA	NA
A = Slight glazed appearance	XX (XX.X%)					
B = Marked glazing	XX (XX.X%)					
C = Glazing with peeling and cracking	XX (XX.X%)					
D = Glazing with fissures	XX (XX.X%)					
E = Film of dried serous exudates	XX (XX.X%)					
F = Small petechial erosions and/or scabs	XX (XX.X%)					
G = No other effects	XX (XX.X%)					
Week 2	XX	XX	XX	XX	XX	XX
A = Slight glazed appearance	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Continue for the following study visits, applicable to Cohort 2 only: Week 4, Week 8, and Week 12; put "NA" in the study visit row for Cohort 1 for these visits.

Abbreviations: BID = twice daily; NA = not applicable; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received, study visit, and overall*100. The Week 1 study visit is only applicable to Cohort 1 subjects; the Week 4 through Week 12 study visits are only applicable to Cohort 2 subjects. These assessments should be done prior to the study drug application in the study site. Subjects not meeting this condition on baseline visit are completely removed from the table summary. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.9.1

Table 14.3.6.2.1
Cohorts 1 and 2: Summary of Subject Local Tolerability Assessment by Study Visit
Safety Population

(Same shell as Table 14.3.6.1.1; use the below footnotes)

Abbreviations: BID = twice daily; NA = not applicable; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. The Week 1 study visit is only applicable to Cohort 1 subjects; the Week 2 through Week 12 study visits are only applicable to Cohort 2 subjects. These assessments should be done 10 - 15 minutes after the application of study drug at the study site. Subjects not meeting this condition on baseline visit are completely removed from the table summary. Baseline is the first non-missing measurement taken after the first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.9.2

Table 14.3.6.2.2
Cohorts 1 and 2: Summary of Subject Local Tolerability Assessment by Study Visit
Categorical Results
Safety Population

Study Visit Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% BID (N=XX)	Cohort 2 ARQ-252 Cream 0.1% QD (N=XX)	Cohort 2 Vehicle Cream QD (N=XX)	Cohort 2 Vehicle Cream BID (N=XX)
Baseline	XX	XX	XX	XX	XX	XX
0 = None (no sensation)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 = Mild (slight warm, tingling sensation)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2 = Moderate (definite warm, tingling sensation)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 = Severe (hot, tingling/stinging sensation)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 1	XX	NA	NA	NA	NA	NA
0 = None (no sensation)	XX (XX.X%)					
1 = Mild (slight warm, tingling sensation)	XX (XX.X%)					
2 = Moderate (definite warm, tingling sensation)	XX (XX.X%)					
3 = Severe (hot, tingling/stinging sensation)	XX (XX.X%)					
Week 2	XX	XX	XX	XX	XX	XX
0 = None (no sensation)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Continue for the following study visits, applicable to Cohort 2 only: Week 4, Week 8, and Week 12; put "NA" in the study visit row for Cohort 1 for these visits.

Abbreviations: BID = twice daily; NA = not applicable; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received, study visit, and overall*100. The Week 1 study visit is only applicable to Cohort 1 subjects; the Week 4 through Week 12 study visits are only applicable to Cohort 2 subjects. These assessments should be done 10 - 15 minutes after the application of study drug at the study site. Subjects not meeting this condition on baseline visit are completely removed from the table summary. Baseline is the first non-missing measurement taken after the first application of study drug.
Reference Listing: 16.2.9.2

Table 14.3.6.3.1
Cohort 1: Summary of Vital Signs by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.1; study visits include Baseline, Week 1, Week 2, and Week 3; parameters include Temperature (°C), Heart Rate (bpm), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Height (cm), Weight (kg), and Body Mass Index (kg/m^2) [1]; use the below footnotes)

Abbreviation: QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Body Mass Index (BMI) = weight (kg) / [height (m)]^2.
Reference Listing: 16.2.9.3

Table 14.3.6.3.2
Cohort 2: Summary of Vital Signs by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.2; study visits include Baseline, Week 2, Week 4, Week 8, Week 12, and Week 13; parameters include Temperature (°C), Heart Rate (bpm), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Height (cm), Weight (kg), and Body Mass Index (kg/m^2) [1]; use the below footnotes)

Abbreviations: BID = twice daily; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Body Mass Index (BMI) = weight (kg) / [height (m)]^2.
Reference Listing: 16.2.9.3

Table 14.3.6.4.1.1
Cohort 1: Summary of 12-Lead Electrocardiogram by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.1; study visits include Baseline and Week 2; parameters include PR Interval (msec), QRS Interval (msec), QT Interval (msec), QTcF Interval (msec), and Heart Rate (bpm); use the below footnotes)

Abbreviation: QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Baseline is the last non-missing measurement taken before the first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.9.4

Table 14.3.6.4.1.2
Cohort 2: Summary of 12-Lead Electrocardiogram by Study Visit
Safety Population

(Same shell as Table 14.3.5.1.1.2; study visits include Baseline, Week 4, and Week 12; parameters include PR Interval (msec), QRS Interval (msec), QT Interval (msec), QTcF Interval (msec), and Heart Rate (bpm); use the below footnotes)

Abbreviations: BID = twice daily; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Baseline is the last non-missing measurement taken before the first application of study drug. Change from baseline is calculated as result – baseline result.
Reference Listing: 16.2.9.4

Table 14.3.6.4.2.1
Cohort 1: Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Safety Population

Study Visit Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Baseline	
Normal	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)
Missing	XX (XX.X%)
Total	XX (XX.X%)
Week 2	
Normal	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)
Missing	XX (XX.X%)
Total	XX (XX.X%)

Abbreviation: CS = clinically significant; NCS = not clinically significant;
QD = once daily.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.9.4

Table 14.3.6.4.2.2
Cohort 2: Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Safety Population

	Cohort 2				
Study Visit Category	ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Baseline					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 4					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Week 12					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: BID = twice daily; CS = clinically significant; NCS = not clinically significant; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken before the first application of study drug.
Reference Listing: 16.2.9.4

Table 14.3.6.5.1
Cohort 1: Summary of Physical Examination by Study Visit
Safety Population

Study Visit Body System Category	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Screening	
Skin	
Normal	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)
Missing	XX (XX.X%)
Total	XX (XX.X%)
Lungs	
Normal	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)
Missing	XX (XX.X%)
Total	XX (XX.X%)
Heart	
Normal	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)
Missing	XX (XX.X%)
Total	XX (XX.X%)

Repeat for Baseline, Day 8, Week 2, and Week 3.

Abbreviations: CS = clinically significant; NCS = not clinically significant;
QD = once daily.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
Reference Listing: 16.2.9.5

Table 14.3.6.5.2
Cohort 2: Summary of Physical Examination by Study Visit
Safety Population

Study Visit Body System Category	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	ARQ-252 Cream 0.3% BID (N=XX)	ARQ-252 Cream 0.1% QD (N=XX)	Vehicle Cream QD (N=XX)	Vehicle Cream BID (N=XX)
Screening					
Skin					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lungs					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Heart					
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (NCS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal (CS)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Repeat for Baseline and Week 12.

Abbreviations: BID = twice daily; CS = clinically significant; NCS = not clinically significant; QD = once daily.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Baseline is the last non-missing measurement taken on or before the day of first application of study drug.
Reference Listing: 16.2.9.5

Table 14.3.6.6
Cohorts 1 and 2: Summary of Concomitant Medications by ATC Class Level 4 and Preferred Term
Safety Population

ATC Class Level 4 Preferred Term	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)	 Vehicle Cream QD (N=XX)	 Vehicle Cream BID (N=XX)
Subjects with at least 1 Concomitant Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: ATC = Anatomic Therapeutic Chemical; BID = twice daily; PT = preferred term; QD = once daily; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Percentages are n/Number of subjects in the Safety population within treatment received*100. Medications were coded using WHO-DDE Global B3 version September 2019.
Concomitant medications are all medications that were continuing or starting after first application of study drug. Medications are displayed by alphabetical order of ATC Level 4 classification, then descending frequency of PT within ATC, and then alphabetically by PT. Subjects were counted only once for each ATC and PT.
[1] ATC Level 4 was not definable for these preferred terms due to multiple ingredients that cannot be mapped to an ATC Level 4 term, route of administration and indication that is not defined in an ATC Level 4 term, or some similar circumstance.
Reference Listing: 16.2.9.7

Programming note: *ATC & PT text should be presented as is from the dataset. If medications are coded but are missing ATC Class Level 4, display as "NOT DEFINED [1]" in the ATC Class Level 4 row and include footnote [1]; otherwise remove footnote [1] from the table.*

Table 14.4.1.1
Cohort 1: Summary of Pharmacokinetic Results by Study Visit and Time Point
PK Population

Study Visit Time Point Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Day 1	
Predose	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX
1 hour postdose	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX
2 hours postdose	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX
4 hours post dose	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX
Repeat for Day 1: 4 hours postdose, 6 hours postdose, and 24 hours postdose; Day 8: Predose; Week 2: Predose, 1 hour postdose, 2 hours postdose, 4 hours postdose, 6 hours postdose, and 24 hours postdose.	

Abbreviations: QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Results at any predose time points that occurred after dosing are excluded from this summary.
Reference Listings: 16.2.5.6.1, 16.2.5.6.2

Table 14.4.1.2
Cohort 2: Summary of Pharmacokinetic Results by Study Visit and Time Point
PK Population

Study Visit Time Point Statistic	Cohort 2 ARQ-252 Cream 0.3% QD (N=XX)	 ARQ-252 Cream 0.3% BID (N=XX)	 ARQ-252 Cream 0.1% QD (N=XX)
Day 1			
Predose			
n	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Week 4			
Predose			
n	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Week 12			
Predose			
n	XX	XX	XX
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX

Abbreviations: BID = twice daily; QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received. Results at any predose time points that occurred after dosing are excluded from this summary.
Reference Listings: 16.2.5.6.1, 16.2.5.6.2

Table 14.4.2
Cohort 1: Summary of Pharmacokinetic Parameters by Study Visit
PK Population

Parameter: XXXXXXXXXXX (unit)

Study Visit Statistic	Cohort 1 ARQ-252 Cream 0.3% QD (N=XX)
Day 1	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX
Week 2	
n	XX
Mean (SD)	XX.X (X.XX)
Median	XX.X
Min, Max	XX, XX

Abbreviations: QD = once daily; SD = standard deviation.
Note: Subjects are summarized by treatment received.
Reference Listing: 16.2.5.7

14.3. Planned Listing Shells

Listing 16.2.1.1
Subject Disposition
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Did Subject Complete Study?	Date of Completion/ Early Termination (Study Day)	Reason for Early Termination	Date of Death/ Cause of Death	Early Termination due to COVID-19 Disruption	Date of Last Dose (Study Day)
XXXX	XXXXX	Yes	DDMMMYYYY (XX)			XX	DDMMMYYYY (XX)
XXXX	XXXXX	Yes	DDMMMYYYY (XX)			XX	DDMMMYYYY (XX)
XXXX	XXXXX	Yes	DDMMMYYYY (XX)			XX	DDMMMYYYY (XX)
XXXX	XXXXX	Ongoing					
XXXX	XXXXX	No	DDMMMYYYY (XX)	XXXXXX	DDMMMYYYY / XXXXXXX	XX	DDMMMYYYY (XX)

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.

Programming note: *If reason for early termination is Other, concatenate the specify text as follows: "Other: XXXXXXXXX".*

Listing 16.2.1.2
Subject Visits
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Visit Performed?	Study Visit	Visit Date (Study Day)	If Visit not Performed, COVID-19 Disruption Contributed to Missed Visit
XXXXXX	XXXXXX	Yes	XXXXXXX	DDMMMYYYY (XX)	
		Yes	XXXXXX	DDMMMYYYY (XX)	
		Yes	XXXXXXXXX	DDMMMYYYY (XX)	
		No	XXXXXXX		Yes
XXXXXX	XXXXXX	Yes	XXXXXXX	DDMMMYYYY (XX)	
		Yes	XXXXXX	DDMMMYYYY (XX)	

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Listing 16.2.2.1
Inclusion and Exclusion Criteria
All Subjects

Cohort: Cohort x

Subject ID	Subject Screen Failed due to COVID-19 Disruption	Treatment [1]	Date/Time (Study Day) of: Screening	Informed Consent	All Inclusion Criteria Met? [2]	Any Exclusion Criteria Met? [3]
XXXXXX	XX	XXXXXX	DDMMMYYYY (-X)	DDMMMYYYY/hh:mm (-X)	Yes	No
XXXXXX	XX		DDMMMYYYY	DDMMMYYYY/hh:mm	No: 02, 10	No
XXXXXX	XX		DDMMMYYYY	DDMMMYYYY/hh:mm	No: 01	No
XXXXXX	XXX	XXXXXX	DDMMMYYYY (-X)	DDMMMYYYY/hh:mm (-X)	Yes	Yes: 03
XXXXXX	XX	XXXXXX	DDMMMYYYY (-X)	DDMMMYYYY (-X)	Yes	No
XXXXXX	XX	XXXXXX	DDMMMYYYY (-X)	DDMMMYYYY (-X)	Yes	No

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] 01 = Participants legally competent to sign and give informed consent; 02 = Males and females 18 years of age and older (inclusive) at the time of consent; 10 = Subjects are considered reliable and capable of adhering to the Protocol and visit schedule according to the Investigator judgment.
[3] 03 = Subjects with any presence or history of psoriasis.

Programming note: *If more than 1 inclusion or exclusion criterion number exists, concatenate with a comma as shown above. Decode any relevant criteria in the footnotes as shown in the example. If no criteria are present for a column, remove the [2] and/or [3] from the column header. Time is only collected for informed consent. If time is missing, display as shown in the shell.*

Listing 16.2.2.2
Protocol Deviations
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Event Type	Violation Level [2]	Description	COVID-19 Related	COVID-19 Infection	Action/Resolution
XXXXXX	XXXXXX	XXXXXXXXXXX XXXXXXXXXXXXX X	XXXXXX XXXXXX *	XXXXXXX XXXXXXXXXXXXXXX	XXX XXXX	XXX XXXX	XXXXXXX XXXXXXX
XXXXXX	XXXXXX	XXXXXXXXXXXX XXXXXXXXXXXXX XX	XXXXXX XXXXXX	XXXXXXXXXXXXXXXXXXX XXXXXXXXXXX	XXXX XXXX	XXXX XXXX	XXXXXXX XXXXXXX
XXXXXX	XXXXXX	XXXXXXXXXXXX	XXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXX	XXXX	XXXXXXX

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
[1] Treatment received for both cohorts.
[2] * = led to exclusion from Per Protocol population.

Programming note: *The structure of this listing may change depending on the information in the protocol deviations file. If a PD is responsible for exclusion from PP population, concatenate violation level with a * as shown above.*

Listing 16.2.3.1
Subject Randomization
All Subjects

Cohort: Cohort x

		Randomization			
Subject ID	Treatment [1]	Randomized Treatment	Date/Time	Number	Stratification ID
XXXXXX	XXXXXX	XXXXX	DDMMMYYY/ hh:mm	XXXX	XXXX
XXXXXX	XXXXXXX	XXXXX	DDMMMYYY/ hh:mm	XXXX	XXXX
XXXXXX					

Abbreviation: BID = twice daily; QD = once daily.
[1] Treatment received for both cohorts.

Listing 16.2.3.2
Analysis Populations
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Safety [2]	All Treated [3]	ITT [4]	PP [5]	PRU4 [6]	PNRS4 [7]	PNRS3 [8]	PNRS2 [9]	ND [10]	PK [11]	Primary Reason(s) for Exclusion [12]
XXXXXX	XXXXXX	Yes	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	
XXXXXX	XXXXXXX	Yes	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	
XXXXXX		No	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	Subject did not receive at least 1 dose of IP.

Abbreviations: BID = twice daily; ITT = intent-to-treat; IP = investigational product; NA = not applicable; ND = nail dystrophy; NRS = Numeric Rating Scale; PK = pharmacokinetic; PRU4 = Subjects with WI-NRS Pruritus Score ≥4 at Baseline; PNRS2 = Subjects with Pain NRS Score ≥2 at Baseline; PNRS3 = Subjects with Pain NRS Score ≥3 at Baseline; PNRS4 = Subjects with Pain NRS Score ≥4 at Baseline; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
[1] Treatment received for both cohorts.
[2] The Safety Population includes all subjects who are enrolled and received at least 1 confirmed dose of IP.
[3] The All Treated Population includes all subjects in the Safety population in Cohort 1.
[4] The ITT Population includes all subjects who are randomized to Cohort 2.
[5] The PP population includes all subjects in the Safety population in Cohort 2, who were at least 80% compliant with study medication application, and showed no important deviations from the study protocol that would affect the interpretation of efficacy.
[6] The PRU4 population is a subset of the ITT population and includes subjects with WI-NRS pruritus score ≥ 4 at Baseline. This population is used for the analyses of achievement of a 4-point reduction in WI-NRS pruritus score as compared to Baseline.
[7] The PNRS4 population is a subset of the ITT population and includes subjects with Pain NRS score ≥ 4 at Baseline. This population is used for the analyses of achievement of a 4-point reduction in Pain NRS pruritus score as compared to Baseline.
[8] The PNRS3 population is a subset of the ITT population and includes subjects with Pain NRS score ≥ 3 at Baseline. This population is used for the analyses of achievement of a 3-point reduction in Pain NRS pruritus score as compared to Baseline.
[9] The PNRS2 population is a subset of the ITT population and includes subjects with Pain NRS score ≥ 2 at Baseline. This population is used for the analyses of achievement of a 2-point reduction in Pain NRS pruritus score as compared to Baseline.
[10] The ND population is a subset of the ITT population and includes subjects with nail dystrophy at Baseline. This population is used for the analyses of nail dystrophy as compared to Baseline.
[11] The PK population includes all subjects receiving the active drug with sufficient plasma concentrations of ARQ-254 to define a profile, as determined by the pharmacokineticist.
[12] Applies to the Safety, ITT, and PP populations only.

Listing 16.2.4.1.1
Subject Demographics
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Sex	Child-Bearing Potential? If Yes, Specify Contraception	Is Subject Post Menopausal?	Year of Birth	Age (years)	Ethnicity	Race	Was Photography Consent Obtained?	Photography Consent Date
XXXXX X	XXXXXX	XXXXX	No	Yes	YYYY	XX	XXXXX X	XXXXX X	Yes	DDMMMYYYY
XXXXX X	XXXXXX	XXXXX	No	Yes	YYYY	XX	XXXXX X	XXXXX X	Yes	DDMMMYYYY
XXXXX X	XXXXXX	XXXX			YYYY	XX	XXXXX X	XXXXX X	No	
XXXXX X	XXXXXX	XXXX			YYYY	XX	XXXXX X	XXXXX	Yes	DDMMMYYYY
XXXXX X	XXXXXX	XXXXX	No	Yes	YYYY	XX	XXXXX X	XXXXX X	Yes	DDMMMYYYY
XXXXX X	XXXXXX	XXXXX	Yes: XXXXXXX; XXXX	No	YYYY	XX	XXXXX X	XXXXX X	XXX	DDMMMYYYY

Abbreviations: BID = twice daily; QD = once daily.
Note: Age at Screening.
[1] Treatment received for both cohorts.

Programming note: *If subject has multiple races, concatenate them. If child-bearing potential is Yes, concatenate type of contraception with ":" as shown in the shell. Concatenate method of contraception and type of barrier method if answered, as shown in the shell with ";".*

Listing 16.2.4.1.2
Baseline Characteristics
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Height (cm)	Weight (kg)	Total Hand BSA (%)	IGA [2]	WI-NRS [3]	Pain NRS [3]	HECSI Total Score [2]	QOLHEQ Total Score [2]	Nail with Worst Dystrophy [2]
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX	XX	XX	XX	XX	XXXXX
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX *	XX	XX	XX	XX	XXXX
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX	XX	XX	XX	XX	XXXX
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX	XX	XX	XX	XX	XXXXX
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX	XX	XX	XX	XX	XXXXX
XXXXXX	XXXXXX	XX.X	XX.X	XX.X	X = XXXXX	XX	XX	XX	XX	XXXX

Abbreviations: BID = twice daily; BSA = body surface area; HECSI = Hand Eczema Severity Index; IGA = investigator global assessment; N/A = not applicable; NRS = Numeric Rating Scale; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: % BSA affected by disease are the values at Screening. Height and Weight are the values at Baseline Day 1.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] Baseline result, where baseline is the last non-missing measurement taken on or before the day of first application of study drug. * = Screening visit was used as baseline.
[3] Baseline result, where baseline is the last non-missing measurement taken before the day of first application of study drug.

Programming note: *For efficacy scores, if VISIT is not Baseline Day 1 for the record where ABLFL=Y, then add a * to the end of the concatenated numeric + text result, as shown in the shell.*

Listing 16.2.4.2.1
Medical History
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)
XXXXXX	XXXXXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
XXXXXX	XXXXXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing

Abbreviations: BID = twice daily; MedDRA = Medical Dictionary for Regulatory Activities; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. Medical history was coded using MedDRA version 23.0. Only subjects with medical history recorded are listed.
[1] Treatment received for both cohorts.

Programming note: *SOC & PT text should be presented as is from the dataset.*

Listing 16.2.4.2.2
Chronic Hand Eczema Medical History
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Morphologic Subtype of Hand Eczema	Subject Patch Tested Anytime?	Patch Test Result	Date of Patch Test (within past 3 years of Baseline)/ Result	Distribution		
						Surface of Hand	Left Hand	Right Hand
XXXXX X	XXXXXX	XXXXX	Yes	XXXXXX	DDMMMYYYY / Negative	Palmar [2]	XXXXXX	XXXXXX
						Dorsal	XXXXXX	XXXXXX
						Interdigital	XXXXXX	XXXXXX
						Pulpitis	XXXXXX	XXXXXX
XXXXX X	XXXXXX	XXXXX	Yes	XXXX: XXX	DDMMMYYYY / Negative	Palmar [2]	XXXXXX	XXXXXX
						Dorsal	XXXXXX	XXXXXX
						Interdigital	XXXXXX	XXXXXX
						Pulpitis	XXXXXX	XXXXXX
XXXXX X	XXXXXX	XXXX	Yes	XXXXXX	DDMMMYYYY / Negative	Palmar [2]	XXXXXX	XXXXXX
						Dorsal	XXXXXX	XXXXXX
						Interdigital	XXXXXX	XXXXXX
						Pulpitis	XXXXXX	XXXXXX

Abbreviations: BID = twice daily; QD = once daily.
[1] Treatment received for both cohorts.
[2] Including lateral aspects of fingers.

Programming note: *If subject was patch tested anytime and the result is positive, concatenate the specify result ":" as shown in the shell.*

Listing 16.2.5.1
Study Drug Application at the Study Site
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Study Drug Application Performed at Study Site?	COVID-19 Caused Delay/ Missed IP Application	Study Visit	Date/Time of Application (Study Day)	Pre-Application Tube Weight (g)/ Post-Application Tube Weight (g) Measurement	Applied Dose (g)	Reason Pre- and/or Post-Application Tube Weight Measurement not Performed	Kit/Lot Number/ Tube ID
XXXX	XXXXXX	Yes	Yes/ No	XXXX	DDMMMYYYY/HH:MM (X)	XX	XX		XX/ XX
			Yes/ No	XXXX	DDMMMYYYY/HH:MM (X)	XX.X	XX.X		XX/ XX
			No/ No	XXXX	DDMMMYYYY/HH:MM (X)	XX	XX		XX/ XX
		No: XXXXXX	Yes/ Yes	XXXX					
XXXX	XXXXXX	Yes	Yes/ No	XXXX	DDMMMYYYY/HH:MM (X)	XX	XX		XX/ XX
			Yes/ No	XXXX	DDMMMYYYY/HH:MM (X)	XX	XX.X		XX/ XX
			Yes/ No	XXXX	DDMMMYYYY/HH:MM (X)	Not Done		XXXXXXXXX	

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Programming note: *If there is delay or missed IP application due to COVID-19, display as shown in the shell. Concatenate reason not done with ":" as shown in the shell.*

Listing 16.2.5.2
Study Drug Accountability
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Lot/Kit Number/ Tube ID	Tube Dispensed? Reason if No	Date Dispensed (Study Day)	Dispense Weight (g)	Tube Returned? Reason if No	Date Returned (Study Day)	Return Weight (g)
XXXXX	XXXXXX	XXXXX/ XX	Yes	DDMMMYYYY (X)	XX.X	Yes	DDMMMYYYY (X)	XX.X
		XXXXX/ XX	Yes	DDMMMYYYY (X)	XX.X	Yes	DDMMMYYYY (X)	XX.X
		XXXXX/ XX	Yes	DDMMMYYYY (X)	ND	Yes	DDMMMYYYY (X)	ND
XXXXX	XXXXXX	XXXXX	No: XXXXX			No: XXXXX		

Abbreviations: BID = twice daily; ND = not done; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Programming note: *Within subject, sort by dispense date, return date, lot number and Tube ID.*

Listing 16.2.5.3
Diary Dispensation
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Diary Dispensation Visit	Diary Dispensed?	Date Dispensed (Study Day)	Diary Returned Visit	Diary Returned and Reviewed?	Reason Diary not Returned	Date Returned (Study Day)	Date of Last Dose
XXXXX	XXXXXX	XXXXXX	Yes	DDMMMYYYY (X)	XXXXXX	Yes		DDMMMYYYY (X)	DDMMMYYYY (X)
		XXXXXX	Yes	DDMMMYYYY (X)	XXXXXX	Yes		DDMMMYYYY (X)	DDMMMYYYY (X)
		XXXXXX	Yes	DDMMMYYYY (X)	XXXXXX	No	XXXXXXXXXX		
XXXXX	XXXXXX	XXXXX	No		XXXXXX	No	XXXXXXXXX		DDMMMYYYY (X)

Abbreviations: BID = twice daily; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Listing 16.2.5.4
Compliance (CRF)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Study Visit [2]	Subject Compliant with Medication? [2]	Non-Compliance due to COVID-19? [2]	Date of Compliance Check (Study Day) [2]	Compliance [2]	Overall Compliance [3]	Was Subject Retrained if not Compliant with Medication [2]
XXXXXX	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY (X)	XX.X %	XX.X %	
		XXXXXX	XXX	XX	DDMMMYYYY (X)	XX.X %		
		XXXXXX	XXX	XX	DDMMMYYYY (X)	XX.X %		
XXXXXX	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY (X)	XX.X %	XX.X%	
		XXXXXX	XXX	XX	DDMMMYYYY (X)	XX.X %		
		XXXXXX	XX	XX				XXX

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; CRF = case report form; IP = investigational product; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.
[2] This data comes from CRF page and was only collected for subjects in Cohort 2.
[3] Overall compliance will be calculated based on number of applications divided by the expected number of IP applications for each subject. For BID dosing, the expected number of IP applications for each subject is 30 (Cohort 1) or 170 (Cohort 2 BID) for subjects who completed the study or number of days between first and last application of IP, derived as 2 * (last treatment date - first treatment date + 1), for subjects who discontinued early from the study. For QD dosing, the expected number of IP applications for each subject is 85 (Cohort 2 QD) for subjects who completed the study or number of days between first and last application of IP, derived as (last treatment date - first treatment date + 1), for subjects who discontinued early from the study. Number of IP applications is calculated as number of expected IP applications – missed IP applications as collected in the CRF.

Programming note: *Populate overall compliance only for the first visit.*

Listing 16.2.5.5.1
Study Drug Interruption (QD)
All Subjects

Subject ID	Treatment [1]	Study Visit	Date of Missed Dose (Study Day)	Missed Dose due to COVID-19 Disruption?	Reason for Missed Dose
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY (X)	No	XXXXXXXXXXXXXX
		XXXXXX	DDMMMYYYY (X)	No	XXXXXXXXXXXXXX
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY (X)	Yes	XXXXXXXXXXXXXX
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY (X)	No	XXXXXXXXXXXXXX
		XXXXXX	DDMMMYYYY (X)	No	XXXXXXXXXXXXXX

Abbreviations: COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. Study Visit corresponds to the visit where the missed dose was recorded in the case report form.
[1] Treatment received for both cohorts.

Listing 16.2.5.5.2
Study Drug Interruption (BID)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Study Visit	Date/Time of Missed Dose (Study Day)	Missed Dose Timing	Missed Dose due to COVID-19 Disruption?	Reason for Missed Dose
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY/HH:MM (X)	AM	No	XXXXXXXXXXXXXX
		XXXXXX	DDMMMYYYY/HH:MM (X)	PM	No	XXXXXXXXXXXXXX
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY/HH:MM (X)	AM	Yes	XXXXXXXXXXXXXX
XXXXXX	XXXXXX	XXXXXX	DDMMMYYYY/HH:MM (X)	AM	No	XXXXXXXXXXXXXX
		XXXXXX	DDMMMYYYY/HH:MM (X)	PM	No	XXXXXXXXXXXXXX

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19.
Note: Study day is calculated relative to the date of first application of study drug. Study Visit corresponds to the visit where the missed dose was recorded in the case report form.
[1] Treatment received for both cohorts.

Listing 16.2.5.6.1
Cohort 1: Pharmacokinetic Sample Collection
PK Population

Cohort: Cohort x

Subject ID	Treatment [1]	Study Visit	PK Collection Time Point	PK Sample Collected Pre-Dose	PK Sample collected? Reason if No	If Assessment Performed, COVID-19 Contributed to Delay in Assessment	Date/Time of Assessment (Study Day)	Date/Time of Last IP Application [2] (Study Day)	Accession Number	ARQ-252 Concentration (unit)
XXXX X	XXXXX	XXXXXX	XXXXXX	XXX	XXX	XXX	DDMMMYYY/ HH:MM (X)	DDMMMYYY/ HH:MM (X)	XXXXX	XX.X
			XXXXXX	XXX	XXX	XXX	DDMMMYYY/ HH:MM (X)	DDMMMYYY/ HH:MM (X)	XXXXX	XX.X
			XXXXXX	XXX	XXX	XXX			XXXXX	XX.X
			XXXXXX	XX	XX: COVID-19 Disruption	XXX				
			XXXXXX	XX	XX: XXXXXX	XXX				

Abbreviations: BID = twice daily; BLQ = Below the limit of quantification; COVID-19 = novel coronavirus disease-19; IP = investigational product; PK = pharmacokinetic; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for Cohort 1.
[2] Prior to the PK collection.

Programming note: *Only cohort 1 subjects are presented in this listing. If the subject missed PK sample collection due to COVID or any other reason, concatenate reason not done as shown in the shell.*

Listing 16.2.5.6.2
Cohort 2: Pharmacokinetic Sample Collection
PK Population

(Same shell as Listing 16.2.5.6.2; use the below footnotes)

Abbreviations: BID = twice daily; BLQ = Below the limit of quantification; COVID-19 = novel coronavirus disease-19; IP = investigational product; PK = pharmacokinetic; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for Cohort 2.

Programming note: *Only cohort 2 subjects are presented in this listing. If the subject missed PK sample collection due to COVID or any other reason, concatenate reason not done as shown in the shell.*

Listing 16.2.5.7
Cohort 1: Pharmacokinetic Calculated Parameters
PK Population

Subject ID	Treatment [1]	Study Visit	Analyte	AUC_{0-t} (unit)	T_{max} (unit)	C_{max} (unit)
XXXXX	XXXXXX	XXXXXX	XXXXXX	XX	XX	XX
			XXXXXX	XX	XX	XX
			XXXXXX	XX	XX	XX
		XXXXXX	XXXXXX	XX	XX	XX

Abbreviations: BID = twice daily; PK = pharmacokinetic.
[1] Treatment received.

Programming note: *The above parameters are expected. However the final parameters provided by the pharmacokineticist will be listed and may be different than shown.*

Listing 16.2.6.1
Investigator Global Assessment (IGA)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Completed?	Study Visit	Date of Assessment (Study Day)	Result	Text Result	Change from Baseline	IGA Score of "Clear" or "Almost Clear" [2]	IGA Success [3]
XXXX	XXXXXX	Yes	XXXX	DDMMMYYYY (X)	X	XXXXXX			
		Yes	XXXX	DDMMMYYYY (X)	X	XXXXXX	X	No	No
		Yes: COVID-19 Disruption Caused/Contributed to Delay in IGA Collection	XXXX	DDMMMYYYY (X)	X	XXXXXX	X	No	No
		Yes	XXXX	DDMMMYYYY (X)	X	XXXXXX	X	Yes	Yes
XXXX	XXXXXX	No: COVID-19 Disruption Caused/Contributed to Missed IGA Collection	XXXX	DDMMMYYYY (X)	X	XXXXXX			
		No: XXXXXXXX	XXXX						

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] IGA Score of "Clear" or "Almost Clear" ("Yes") is defined as an IGA score of "Clear" or "Almost Clear"; "No" otherwise.
[3] IGA Success ("Yes") is defined as an IGA score of "Clear" or "Almost Clear" plus a ≥2-grade improvement from baseline; "No" otherwise.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in IGA Collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in IGA Collection"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed IGA Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed IGA Collection"; if reason IGA not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed IGA Collection; XXXXXXXXXX"
"No: XXXXXXXXXXX'

Listing 16.2.6.2
Worst Itch Numerical Rating Scale (WI-NRS)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Completed?	Study Week	Date of Assessment (Study Day)	Result	Change from Baseline	WI-NRS Success (Baseline ≥ 4) [2]
XXXXXX	XXXXXX	Yes	Baseline	DDMMMYYYY (-1)	X		
		Yes	Week 1	DDMMMYYYY (1)	X	X	
		Yes		DDMMMYYYY (2)	X	X	
		Yes		DDMMMYYYY (3)	X	X	
		Yes		DDMMMYYYY (4)	X	X	
		Yes		DDMMMYYYY (5)	X	X	
		Yes		DDMMMYYYY (6)	X	X	
		Yes		DDMMMYYYY (7)	X	X	
				…			
		Yes	Week 2	DDMMMYYYY (14)	X	X	
					Average Weekly Score: X [3]	X	Yes
		Yes	Week X	DDMMMYYYY (X)	X	X	
		No: COVID-19 Disruption		DDMMMYYYY (X)	X	X	
XXXXXX	XXXXXX	Yes	XXXX	DDMMMYYYY (X)	X		
		No: XXXXXX	XXXX				

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily; WI-NRS = Worst Itch – Numeric Rating Scale.
Note: Study day is calculated relative to the date of first application of study drug. Subjects rate the intensity of their itch on an 11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable). Higher score indicates greater itch intensity. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] WI-NRS Success is defined as achievement of a 4-point reduction in WI-NRS pruritus score at each study week compared to baseline, calculated only for subjects with a pruritus score of ≥ 4 at baseline.
[3] Average of the WI-NRS pruritus daily diary scores for each study week. If at least 1 WI-NRS pruritus score in present in this time period, the average weekly WI-NRS pruritus score was calculated.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a missed WI-NRS Collection?" is "Yes", then only display "Yes".*
For "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed WI-NRS Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed WI-NRS Collection"; if reason WI-NRS not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed WI-NRS Collection; XXXXXXXXXX" or "No: XXXXXXXXXXXX"

Listing 16.2.6.3
Hand Eczema Severity Index (HECSI)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Completed?	Study Visit	Date of Assessment (Study Day)	Location	Clinical Signs	Numeric Result	Text Result	Change from Baseline	% Change from Baseline
XXXX	XXXXXX	Yes	XXXXXXX	DDMMMYYYY (XX)	Fingertips	Affected Area	XX	XXXX		
						Erythema	XX	XXXX		
						Infiltration/papulation	XX	XXXX		
						Vesicles	XX	XXXX		
						Fissures	XX	XXXX		
						Scale	XX	XXXX		
						Oedema	XX	XXXX		
						Fingertips Subscore [2]	XX			
					Fingers (except tips)	Affected Area	XX	XXXX		
						…	XX	XXXX		
						Fingers (except tips) Subscore [2]	XX			
					Palm of Hands	Affected Area	XX	XXXX		
						…	XX	XXXX		
						Palm of Hands Subscore [2]	XX			
					Back of Hands	Affected Area	XX	XXXX		
						…	XX	XXXX		
						Back of Hands Subscore [2]	XX			
					Wrists	Affected Area	XX	XXXX		
						…	XX	XXXX		
						Wrists Subscore [2]	XX			
					Total Score [3]		XX			

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; HECSI = Hand Eczema Severity Index; QD = once daily.
Note: Study day is calculated relative to the date of the first application of study drug. The HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] Subscores are calculated as the sum of erythema, infiltration/papulation, vesicles, fissures, scale, and oedema, respectively, scored on a scale of 0 to 3 (none to severe) time is estimated area of skin involved, graded on a scale of 0 to 4, within a location. The range for each subscore is 0 to 72. Lower scores indicate better outcomes.
[3] The total score is calculated as the sum of all subscores. The range for the total score is 0 to 360. Lower scores indicate better outcomes.

Programming note: *Continue for all visits.* ***Programming note:*** *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in HECSI Collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in HECSI Collection"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed HECSI Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed HECSI Collection"; if reason HECSI not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed HECSI Collection; XXXXXXXXXX" or "No: XXXXXXXXXXX"

Listing 16.2.6.4
Pain Numeric Rating Scale (NRS)
All Subjects

(Same shell as Listing 16.2.6.2; change all instances of WI-NRS to Pain NRS; use the below footnotes)

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; NRS = Numeric Rating Scale; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. Subjects rate the worst pain intensity on an 11-point scale ranging from 0 (no pain) to 10 (worst possible pain). Higher score indicates greater pain intensity. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] Pain NRS success is defined as 4-point reduction in Pain NRS score at Weeks 2, 4, 8, or 12 compared to baseline, calculated only for subjects with a Pain NRS score of ≥ 4 at baseline.
[3] Average of the Pain NRS daily diary scores for each study week. If at least 1 Pain NRS score in present in this time period, the average weekly Pain NRS score was calculated.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes, then only display "Yes".*
For "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed NRS Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed Pain NRS Collection"; if reason WI-NRS not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed Pain NRS Collection; XXXXXXXXXX" or "No: XXXXXXXXXXX"

Listing 16.2.6.5
Quality of Life in Hand Eczema Questionnaire (QOLHEQ)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Completed?	Study Visit	Date of Assessment (Study Day)	Question [2]	Result	Text Result	Change from Baseline
XXXX	XXXXXX	Yes	XXXX	DDMMMYYYY/ (XX)	1. Being painful	0	Never	
					2. Restricting/impairing me in my job	1	Rarely	
					3. Restricting/impairing me in doing everyday home duties	2	Sometimes	
					4. Because I have to wear gloves	3	Often	
					5. Making me feel frustrated	0	All the time	
					6. Itching	1	Several days	
					7. Because treatment is time consuming	2	More than half the days	
					----			
					30. making me feel nervous	3	Nearly every day	
					Symptoms Subscore [3]	XX		
					Emotions Subscore [4]	XX		
					Limitations in Functioning Subscore [5]	XX		
					Treatment and Prevention Subscore [6]	XX		
					Total Score [7]	XX		

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily; QOLHEQ = Quality of Life in Hand Eczema Questionnaire.
Note: Study day is calculated relative to the date of the first application of study drug. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result.
[1] Randomized treatment for Cohort 2.
[2] These questions are based on the "Over the last 7 days, how often have you been bothered by any of the skin conditions of my hand?" prompt.
[3] The range for Symptoms subscore is 0 to 27, where lower scores indicate better outcomes.
[4] The range for Emotions subscore is 0 to 31, where lower scores indicate better outcomes.
[5] The range for Limitations in Functioning subscore is 0 to 32, where lower scores indicate better outcomes.
[6] The range for Treatment and Prevention subscore is 0 to 27, where lower scores indicate better outcomes
[7] The QOLHEQ total score is calculated as sum of all 30 questions. The range for Total score is 0 to 117, where lower scores indicate better outcomes.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "If Yes, did COVID-19 disruption cause or contribute to a delay in QOLHEQ Collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in QOLHEQ Collection"; similarly, if the answer to the question "If Yes, did QOLHEQ assessment occur via telemedicine?" is "Yes", set to "Yes: QOLHEQ assessment occurred via telemedicine"; if both are answered "Yes" concatenate them with a semicolon; if answers to both COVID-19 questions are "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed QOLHEQ Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed QOLHEQ Collection"; if reason QOLHEQ not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed QOLHEQ Collection; XXXXXXXXXX" or "No: XXXXXXXXXXXX"

Listing 16.2.6.6
% Body Surface Area (BSA)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Performed?	Study Visit	Date of Assessment (Study Day)	Surface of Hand	Result	Change from Baseline	% Change from Baseline
XXXX	XXXXXX	XXX	XXXX	DDMMMYYYY (XX)	Dorsal % BSA (Left Hand)	XX %		
					Dorsal % BSA (Right Hand)	XX %		
					Palmar % BSA (Left Hand)	XX %		
					Palmar % BSA (Right Hand)	XX.X %		
					Total Hand % BSA [2]	XX.X %		

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of the first application of study drug. Baseline is the last non-missing measurement taken on or before the day of first application of study drug. Change from baseline is calculated as result – baseline result. Percent change from baseline is calculated as (change from baseline/baseline)*100.
[1] Treatment received for Cohort 1 and randomized treatment for Cohort 2.
[2] Total Hand % BSA is calculated as the sum of dorsal % BSA (left hand), dorsal % BSA (right hand), palmar % BSA (left hand), and palmar % BSA (right hand).

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in BSA Collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in BSA Collection"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed BSA Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed BSA Collection"; if reason BSA not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed BSA Collection; XXXXXXXXXX"
"No: XXXXXXXXXXX'

Listing 16.2.6.7
Nail Dystrophy Assessment
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Performed?	Study Visit	Date of Assessment (Study Day)	Subject has at least One Nail with Significant Dystrophy	If Yes, Is there Normal Appearing Nail Distal to the Cuticle	Result (mm)
XXXX	XXXXXX	XXX	XXXX	DDMMMYYYY (XX)	Yes: Left		
			XXXX	DDMMMYYYY (XX)		Yes	XX
			XXXX	DDMMMYYYY (XX)		Yes	XX
			XXXX	DDMMMYYYY (XX)		No	
XXXX	XXXXXX	XXX	XXXX	DDMMMYYYY (XX)	No		
XXXX	XXXXXX	No: XXXXXXX	XXXX				

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of the first application of study drug.
[1] Randomized treatment for Cohort 2.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in Nail Dystrophy Assessment?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in Nail Dystrophy Assessment"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed Nail Dystrophy Assessment?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed Nail Dystrophy Assessment"; if reason Nail Dystrophy Assessment not completed is non-missing, concatenate that reason with the response to "No", as follows: "No: COVID-19 Disruption Caused/Contributed to Missed Nail Dystrophy Assessment; XXXXXXXXXX" or "No: XXXXXXXXXXX"

Listing 16.2.7.1
Adverse Events
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	TEAE?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	CTCAE Toxicity Grade/ Relationship	Outcome/ Action Taken/ Other Action Taken	Serious?	AE Lead to Study D/C?
XXXXX	XXXXXX	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/hh:mm (X)/ DDMMMYYYY/ hh:mm (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XX	XX
XXXXX	XXXXXX	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY/ hh:mm (X)/ DDMONYYYY/ hh:mm (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XX	XX
		XX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXXXXX	DDMONYYYY/ hh:mm (X)/ Ongoing	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX/ XXXXXXXXXX	XXX	XXX

Abbreviations: BID = twice daily; CTCAE = Common Terminology Criteria for Adverse Events; D/C = discontinuation; MedDRA = Medical Dictionary for Regulatory Activities; QD = once daily; TEAE = treatment emergent adverse event.
Note: Study day is calculated relative to the date of first application of study drug. AEs were coded using MedDRA version 23.0. All AEs with an onset on or after the day of study treatment through study completion are considered as TEAEs.
[1] Treatment received for both cohorts.

Programming note: *If time missing, display "- -:- -". "Other Action Taken" will be either None, Concomitant Medication, Non-drug Therapy, Hospitalization or Prolongation of Hospitalization, Discontinued Study or Other; if specify text is needed, concatenate "Concomitant Medication:" or "Other:" with the text. If no events meet the criteria for display, present "No events are reported." SOC & PT text should be presented as is from the dataset.*

Listing 16.2.8.1.1
Clinical Laboratory Data: Clinical Chemistry
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Parameter (unit)	Study Visit	Date/Time of Assessment (Study Day)	Standard Results	Reference Range [2]	Reference Range Flag	Result Interpretation; Specify CS Finding	Accession Number	Comments/ Reason not Done
XXXXX	XXXXX	Alanine Aminotransferase (U/L)	XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY	High	Normal	XXXXX	
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY		Abnormal, NCS	XXXX	
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY	Low	Normal	XXXXX	
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY		Normal	XXXXX	
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY		Abnormal, CS; XXXXXXX	XXXXX	
		Alkaline Phosphatase (U/L)	XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY	Low	XXXXX	XXXXX	
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY		XXXXX	XXXXX	
			XXXXX		ND					XXXXXXX
			XXXXX	DDMMMYYYY/hh:mm (XX)	XX	XX – YY	High	XXXXXX	XXXXX	

Abbreviations: BID = twice daily; CS = clinically significant; NCS = not clinically significant; ND = not done; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. Time is collected in the ACM data.
[1] Treatment received for both cohorts.
[2] Reference range is used to identify potentially clinically significant laboratory values.

Listing 16.2.8.1.2
Clinical Laboratory Data: Hematology
All Subjects

(Same shell as Listing 16.2.8.1.1)

Listing 16.2.8.1.3
Clinical Laboratory Data: Urinalysis
All Subjects

(Same shell as Listing 16.2.8.1.1)

Listing 16.2.8.1.4
Clinical Laboratory Data: TSH/T4
All Subjects

(Same shell as Listing 16.2.8.1.1)

Listing 16.2.8.1.5
Clinical Laboratory Data: Serum and Urine Pregnancy Test
Female Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Pregnancy Test Performed? Reason if No	Study Visit	Type of Test	Date/Time Performed (Study Day)	Result
XXXXX	XXXXXX	Yes	XXXXXX	Serum	DDMMMYYYY (XX)	XXXXXXXX
				Urine	DDMMMYYYY/hh:mm (XX)	XXXXXXXXX
			XXXXXX	Urine	DDMMMYYYY/hh:mm (XX)	XXXXXXXXX
XXXXX	XXXXXX	Yes	XXXXXX	Serum	DDMMMYYYY (XX)	XXXXXXXXX
		No: XXXXXXXXXX	XXXXXX	Urine		

Abbreviations: BID = twice daily; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Programming note: *If time is missing, display it as --:--.*

Listing 16.2.8.1.6
Follicle Stimulating Hormone Test
Female Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Performed? Reason if No	Study Visit	Date of Assessment (Study Day)	Result
XXXXX	XXXXXX	Yes	XXXXXX	DDMMMYYYY (XX)	XXXXX
				DDMMMYYYY (XX)	XXXXX
			XXXXXX	DDMMMYYYY (XX)	XXXXX
XXXXX	XXXXXX	Yes	XXXXXX	DDMMMYYYY (XX)	XXXXX
		No: XXXXXXXXXX	XXXXXX		

Abbreviations: BID = twice daily; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Listing 16.2.9.1
Investigator Local Tolerability Assessments
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Tolerability Assessment Performed?	Study Visit	Date/Time of Assessment (Study Day)	Dermal Response	Other Effects
XXXXX X	XXXXXX	Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
XXXXX X	XXXXXX	Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
XXXXX X	XXXXXX	Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	X = XXXXXXXXX	X = XXXXXXXXX
		No: COVID-19 Disruption	XXXXXX			

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; IP = investigational product; QD = once daily.
Note: Study day is calculated relative to the date of the first application of study drug. This assessment will be conducted by the investigator prior to the application of IP in the study site.
[1] Treatment received for both cohorts.

Programming note: *For "Tolerability Assessment Performed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in assessment collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in Assessment Collection"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Tolerability Assessment Performed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed assessment collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed Assessment Collection"

Listing 16.2.9.2
Subject Local Tolerability Assessments
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Tolerability Assessment Performed?	Study Visit	Date/Time of Assessment (Study Day)	Grade	Sensation Following the Application of IP
XXXXX X	XXXXXX	Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	0 = None	No sensation
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	1 = Mild	Slight warm, tingling sensation; not really bothersome
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	2 = Moderate	Definite warm, tingling sensation that is somewhat bothersome
XXXXX X	XXXXXX	Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	0 = None	No sensation
		Yes	XXXXXX	DDMMMYYYY/hh:mm (XX)	3 = Severe	Hot tingling/stinging sensation that has caused definite discomfort
		No: COVID-19 Disruption	XXXXXX			

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; IP = investigational product; QD = once daily.
Note: Study day is calculated relative to the date of the first application of study drug. This assessment was performed at baseline visit 10 to 15 minutes after the application of IP in the study site.
[1] Treatment received for both cohorts.

Programming note: *For "Tolerability Assessment Performed?" column, if answer is Yes and answer to question "If Yes, did COVID-19 disruption cause or contribute to a delay in assessment collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in Assessment Collection"; similarly, if the answer to the question "If Yes, did assessment occur via telemedicine?" is "Yes", set to "Yes: Assessment occurred via telemedicine"; if both are answered "Yes" concatenate them with a semicolon; if answers to both COVID-19 questions are "No", only display "Yes".*
Similarly, for "Tolerability Assessment Performed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed assessment collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed Assessment Collection"

Listing 16.2.9.3
Vital Signs
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Vital Signs Collected? Reason if No	Study Visit	Date of Assessment (Study Day)	Temp (°C)	Heart Rate (bpm)	Position	Blood Pressure (mmHg)		Height (cm)	Weight (kg)	BMI (kg/m^2)	Abnormal Findings/ Clinically Significant/ Description of Finding
								Systolic	Diastolic				
XXXX	XXXX	Yes	XXXXX	DDMMMYYYY (X)	XX.X	XX	XXXX	XX	XX	XXX	XX.X	XX.X	XX
		Yes	XXXXX	DDMMMYYYY (X)	XX.X	XX	XXXXX	XX	XX		XX.X		
		No: XXXXXX	XXXXX										
		Yes	XXXXX	DDMMMYYYY (X)	XX.X	XX	XXXXX	XX	XX		XX.X	XX.X	XXX/ XXX/ XXXXXXX

Abbreviations: BID = twice daily; BMI = body mass index; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.
[2] BMI is derived as (weight in kg)/[(height in cm/100)^2].

Listing 16.2.9.4
12-Lead Electrocardiogram (ECG)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	ECG Performed? Reason if No	Study Visit	Date/Time of Assessment (Study Day)	Heart Rate (beats/min)	PR (msec)	QRS Interval (msec)	QT Interval (msec)	QTcF (msec)	Findings/ Comments
XXXX	XXXX	Yes	XXXXX	DDMMMYYYY/ hh:mm (X)	XX.X	XX	XXXX	XXX	XX.X	XX
		Yes	XXXXX	DDMMMYYYY/ hh:mm (X)	XX.X	XX	XXXXX		XX.X	
		No: XXXXXX	XXXXX							
		Yes	XXXXX	DDMMMYYYY/ hh:mm (X)	XX.X	XX	XXXXX		XX.X	XXX/ XXXXXXX

Abbreviations: BID = twice daily; CS = clinically significant; ECG = electrocardiogram; NCS = not clinically significant; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Listing 16.2.9.5
Physical Examination
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Physical Examination Performed? Reason if No	Study Visit	Date of Assessment (Study Day)	Body System	Result	Abnormal Findings	Clinically Significant?
XXXXXX	XXXXXXX	Yes	XXXXXXX	DDMMMYYYY (-X)	Skin	Normal		
					Lungs	Abnormal	XXXXXXXX	No
					Heart	Normal		
		Yes	XXXXXXX	DDMMMYYYY (-X)	Skin	Normal		
					Lungs	Abnormal	XXXXXXXX	No
					Heart	Normal		
		No: XXXXXXX	XXXXXXX					

Abbreviations: BID = twice daily; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Programming note: *Concatenate reason not done as shown in the shell.*

Listing 16.2.9.6
Medical Photography
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Photography Performed?	Study Visit	Date of Assessment (Study Day)
XXXXXX	XXXXXX	Yes	XXXXXX	DDMMMYYYY (XX)
		Yes	XXXXXX	DDMMMYYYY (XX)
		Yes	XXXXXX	DDMMMYYYY (XX)
		Yes	XXXXXX	DDMMMYYYY (XX)
		No: XXXXXX	XXXXXX	

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.

Programming note: *For "Photography Performed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in assessment collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in Assessment Collection"; if answer to COVID-19 question is "No", only display "Yes". Similarly, for "Photography Performed?" column, if answer is No and answer to question "If No, and Photograph consent given please specify reason photographs not collected" is "COVID-19 Disruption", then display "No: COVID-19 Disruption Caused/Contributed to Missed Assessment Collection"; if reason assessment collection not completed is non-missing, concatenate that reason with the response to "No", as follows:*
"No: COVID-19 Disruption Caused/Contributed to Missed Assessment Collection; XXXXXXXXXX" or "No: XXXXXXXXXXX"

Listing 16.2.9.7
Prior and Concomitant Medications
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Prior/ Concomitant [2]	Indication	ATC Class (Level 4)/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route/ Frequency
XXXXXX	XXXXXX	Prior	XXXXXXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXX (XXX)	XXXXXXXX/ XXXXXXX
		Both	XXXXXXXX	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing	XXX (XXX)	XXXXXXXX/ XXXXXXX
		Concomitant	XXXXXXX	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXX (XXX)	XXXXXXXX/ XXXXXXX

Abbreviations: ATC = anatomic therapeutic chemical; BID = twice daily; NA = Not applicable; QD = once daily; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Study day is calculated relative to the date of first application of study drug. Medications were coded using WHO-DDE Global B3 version September 2019.
[1] Treatment received in both cohorts.
[2] Prior indicates medication that was started and stopped prior to dosing of study drug. Concomitant indicates medication that started during the treatment period. Both indicates medication that was started prior to dosing of study drug and continued during the treatment period.

Programming note: *If Dose unit, Route or Frequency is Other, display other specify text only (i.e., do not display "Other: XXXXXX" but just "XXXXXX "). Sort by subject, start date, end date, ATC level 4 & PT. ATC & PT text should be presented as is from the dataset.*

Listing 16.2.9.8.1
Hand Washing/Hand Sanitizer Use (QD Dosing)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Cleansing Performed? [2]	Study Visit	Date of Cleansing (Study Day)	Type of Hand Cleansing	Time of First Hand Cleansing Post Study Drug Application
XXXXXX	XXXXXX	Yes	XXXXXX	DDMMMYYYY (XX)	Hand Washing	XXXXXXXX
				DDMMMYYYY (XX)	Hand Washing	XXXXXXXX
				DDMMMYYYY (XX)	Hand Sanitizer	XXXXXXXX
			XXXXXX	DDMMMYYYY (XX)	Hand Sanitizer	XXXXXXXX
		No	XXXXXX			

Abbreviations: QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.
[2] This question is based on the prompt “did any handwashing or hand sanitizer use occur within 4 hours of study drug application since last visit?”

Listing 16.2.9.8.2
Hand Washing/Hand Sanitizer Use (BID Dosing)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Cleansing Performed?	Study Visit	Date of Cleansing (Study Day)	AM/PM Dose	Type of Hand Cleansing	Time of First Hand Cleansing Post Study Drug Application
XXXXXX	XXXXXX	XXX	XXXXXX	DDMMMYYYY (XX)	XX	Hand Washing	XXXXXXXX
				DDMMMYYYY (XX)	XX	Hand Washing	XXXXXXXX
				DDMMMYYYY (XX)	XX	Hand Sanitizer	XXXXXXXX
			XXXXXX	DDMMMYYYY (XX)	XX	Hand Sanitizer	XXXXXXXX
				DDMMMYYYY (XX)	XX	Hand Sanitizer	XXXXXXXX

Abbreviations: BID = twice daily.
Note: Study day is calculated relative to the date of first application of study drug.
[1] Treatment received for both cohorts.
[2] This question is based on the prompt “did any handwashing or hand sanitizer use occur within 4 hours of study drug application since last visit?”

Listing 16.2.9.9
Modified Total Lesion Symptom Score (mTLSS)
All Subjects

Cohort: Cohort x

Subject ID	Treatment [1]	Was Assessment Completed?	Study Visit	Date of Assessment (Study Day)	Item	Result
XXXX	XXXXXX	Yes: COVID-19 Disruption Caused/Contributed to Delay in mTLSS Collection	XXXX	DDMMMYYYY (X)	Erythema	X = XXXXXXXXXX
					Scaling	X = XXXXXXXXXX
					Lichenification/hyperkeratosis	X = XXXXXXXXXX
					Vesiculation	X = XXXXXXXXXX
					Edema	X = XXXXXXXXXX
					Fissures	X = XXXXXXXXXX
					Pruritus/Pain	X = XXXXXXXXXX
		Yes	XXXX	DDMMMYYYY (X)	Erythema	X = XXXXXXXXXX
					…	
XXXX	XXXXXX	No: COVID-19 Disruption Caused/Contributed to Missed mTLSS Collection	XXXX	DDMMMYYYY (X)		
		No: XXXXXXXX	XXXX			

Abbreviations: BID = twice daily; COVID-19 = novel coronavirus disease-19; QD = once daily.
Note: Study day is calculated relative to the date of first application of study drug. The mTLSS was removed from the protocol as of amendment 1 (11May2020), thus not all subjects and visits will be present.
[1] Treatment received for both cohorts.

Programming note: *For "Was Assessment Completed?" column, if answer is Yes and answer to question "Yes, did COVID-19 disruption cause or contribute to a delay in mTLSS Collection?" is "Yes", then display "Yes: COVID-19 Disruption Caused/Contributed to Delay in mTLSS Collection"; if answer to COVID-19 question is "No", only display "Yes".*
Similarly, for "Was Assessment Completed?" column, if answer is No and answer to question "If No, did COVID-19 disruption cause or contribute to missed mTLSS Collection?" is "Yes", then display "No: COVID-19 Disruption Caused/Contributed to Missed mTLSS Collection"; if reason mTLSS not completed is non-missing, concatenate that reason with the response to "No", as follows:
"No: COVID-19 Disruption Caused/Contributed to Missed mTLSS Collection; XXXXXXXXXX"
"No: XXXXXXXXXXX'