STATISTICAL ANALYSIS PLAN

For Interim and Primary Analyses at Week 12

1 TITLE PAGE

Study Title	Vagus Nerve Stimulation Using the SetPoint System for Moderate to Severe Rheumatoid Arthritis: The RESET-RA Study
Protocol Number	SPM-020
ClinicalTrials.gov Identifier	NCT04539964
Investigational Device	The SetPoint System
Study Sponsor's Name and Address	SetPoint Medical, Inc. 25101 Rye Canyon Loop Valencia, CA 91355
Biostatistics and Data Analysis	SetPoint Medical, Inc.

Statistical considerations addressing the impact of COVID-19 on the primary and key secondary endpoints are detailed in Section **10.**

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Revision History

Revision	Revision Date	Summary of Changes
A	01DEC2020	Initial release
B	05MAY2021	• Updated document title to reference that SAP pertains to interim and primary analyses (p. 1) • Updated study title, introduction, description of study design, study visits and assessments and schedule of assessments to include one-way crossover and open-label, long-term follow-up per SPM-020 Rev E (pp. 1, 8, 9, 41, 42) • Added Clinicaltrials.gov identifier (p. 1) • Added abbreviations for MMP3, NRS, PMA, and SAA and removed VAS (pp. 6-7) • Added reference to a separate SAP that details analysis for open-label, long-term follow-up (p.8) • Added that blinding will be maintained until the last enrolled and randomized subject in Stage 2 completes Week 12 assessments and the study database is locked (p. 8) • Added statement that initial 12-week follow-up data along with available long-term safety data will support PMA application (p. 8) • Updated DMC analysis to specify frequency of meetings, the period when closed sessions are relevant and added data type for open sessions and a description of the DMC review process (p. 10) • Added clarification to notes regarding access to study data in Table 3 (p. 12) • Updated description of actions taken in the event stopping rule is triggered (p. 12) • Added the Co-PI Rheumatologist's blinding assessment to Table 4 (p. 13), Section 8.7 (p. 43), Schedule of Assessments (Appendix A, p. 43) and mockup tables (Appendix B) and mockup listings (Appendix C) • Changed final analysis to primary analysis (p. 13) • Changed VAS to NRS (p. 21) • Updated examples of biomarkers to be analyzed (p. 28) • Updated AE relationship categories in table 14.1.3.1 and 14.1.3.3-14.3.6 • Removed "Visit" column from listing mockup 16.1.2.1.2 • Added association with AE/SAE to listing mockup 16.1.2.2 • Updated biomarkers in listing 16.1.2.6.11 and table 14.1.2.18 • Removed "Visit" column from listing mockup 16.1.2.7 • Added mockup listing 16.1.2.8 for device deficiencies • Minor editorial changes made throughout document • Minor spelling, formatting, grammatical and typographical errors fixed throughout document • Updated Section 5.2, Table 4 and table mockups (Appendix B) by deleting the PTE population from the primary and key secondary endpoints

C	29JAN2024	• Updated enrollment from "up to 250 randomized subjects" to "at least 240 and up to 250 randomized subjects" and included information for 240 subjects in power analysis (pp. 9, 10, 12 and 17) • Updates made for consistency with current revision of CLP-001, Clinical Investigational Protocol SPM-020 (The RESET-RA Study) (pp. 9-10) • Updates made for consistency with current version of CLP-003, Data Monitoring Committee Charter for SPM-020 (The RESET-RA Study) (pp. 11 and 13) • Specified the Communication Plan that occurred for Interim Analysis (pp. 12-13) • Added PTE analyses for primary outcome and key secondary outcomes (pp. 14, 16 and Appendix B pp. 9, 19-20) • Clarified missing data approaches (pp. 14, 20, 21, 26) • Generalized language pertaining to software requirements for statistical analysis (p. 15) • Added additional strata for Cochran-Mantel Haenszel test and variables to the MMRM to reflect stratification factors of Stage 1 and 2 subjects (pp. 15-16, 17, table footers throughout Appendix B) • Removed reference to collecting safety data once a subject is withdrawn from the study (p. 16) • Added text to delineate the start of the open label/ long term follow-up period for instances in which a Week 12 assessment date is missing (p. 19) • Limited requirement to set all subsequent visits to treatment failure in the case of rescue with oral steroids considering the relatively limited half-life and averaged use between study visits. (p. 19) • Specified corticosteroid injection rescue conditions (p. 19) • Added detail on methods for calculating and analyzing RAMRIS scores (pp. 31-32) • Removed information on calculation of SF-36 scores and replaced with reference to the same information which is found in the SF-36 User's Manual (p. 32) • Clarified information on calculation of the EQ-5D-5L score (pp. 32-33, Appendix B, pp. 63-67) • Updated description of how AEs are categorized for consistency with study protocol. (pp. 33, Appendix B, p. 87) • Added allowance for adjudication of "stimulation-related" AEs in cases where subject is assigned to control (p. 34) • Added sensitivity analysis for protocol deviations that could potentially bias the primary endpoint assessment (p. 35) • Added additional Covid-19 analyses (Appendix B, pp. 12-13)
D	15JUL2024	• Extended study duration by adding 6 visits as part of open-label, long-term follow-up after completion of Week 12 (pp. 9-11)

2 LIST OF ABBREVIATIONS

Abbreviation	Expansion
ACR	American College of Rheumatology
AE	Adverse event
CARLOS	Cartilage Loss Score
CDAI	Clinical Disease Activity Index
CI	Confidence interval
CMH	Cochran-Mantel-Haenszel
CMO	Chief Medical Officer
CRF	Case report form
CSR	Clinical study report
DAS	Disease Activity Score
DMARD	Disease-modifying antirheumatic drug
DMC	Data monitoring committee
EDC	Electronic data capture
EGA	Evaluator's global assessment
eGFR	Estimated glomerular filtration rate
EQ-5D-5L	EuroQol 5 domains 5 levels
EULAR	European League Against Rheumatism
H_0	Null hypothesis
H_1	Alternate hypothesis
HAQ-DI	Health Assessment Questionnaire Disability Index
hsCRP	High-sensitivity C-reactive protein
IL	Interleukin
IRB	Institutional Review Board
IRT	Interactive response technology
ITT	Intent to treat
JAKi	Janus kinase inhibitors
LDA	Low disease activity
LOCF	Last observation carried forward

Abbreviation	Expansion
MAR	Missing at random
MCID	Minimal clinically important difference
MedDRA	Medical Dictionary for Regulatory Activities
MMP3	Matrix metalloproteinase 3
MMRM	Mixed-effect Model Repeated Measure
MRI	Magnetic resonance imaging
NRI	Non-responder imputation
NRS	Numerical rating scale
OC	Observed case
PCS	Physical component summary
PD	Protocol deviation
PF	Physical functioning
PMA	Premarket Approval
PT	Preferred term
PTE	Per-treatment evaluable
QC	Quality check
RA	Rheumatoid arthritis
RAMRIS	Rheumatoid Arthritis MRI Scoring System
RF	Rheumatoid factor
SAA	Serum amyloid A
SADE	Serious adverse device effect
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Statistical Analysis Software
SD	Standard deviation
SF	Social functioning
SF-36	Short Form Survey with 36 items
SGA	Subject's global assessment
SJC28	Swollen joint count for 28 different joints
SOC	System organ class

Abbreviation	Expansion
SOP	Standard operating procedure
TEAE	Treatment emergent adverse event
TJC28	Tender joint count for 28 different joints
UADE	Unanticipated adverse device effect
USADE	Unanticipated serious adverse device effect
WHO	World Health Organization

3 INTRODUCTION

This document outlines the statistical analysis plan (SAP) for the RESET-RA study conducted by SetPoint Medical under protocol SPM-020 entitled "Vagus Nerve Stimulation Using the SetPoint System for Moderate to Severe Rheumatoid Arthritis: The RESET-RA Study." The SAP specifies the data listings, tabular summaries, and analyses to be performed for the primary, secondary and exploratory endpoints and safety evaluation using the randomized, controlled, double-blind data through Week 12 to support an application for Premarket Approval (PMA).

The data listings, tabular summaries, and analyses to be performed for the exploratory endpoints and long-term safety evaluation using the open-label follow-up data through Week 264 are detailed in a separate SAP (CLP-008). The PMA application will include supporting data on long-term safety for all subjects for whom long-term data are available at the time of application.

3.1 Study Objective

The overall objective of this study is to evaluate the safety and efficacy of the SetPoint System for the treatment of adult patients with active, moderate to severe RA who have had an inadequate response or intolerance to biologic or targeted synthetic DMARDs.

3.2 Study Design

This is an operationally seamless, 2-stage, randomized, sham-controlled, double-blind, multicenter pivotal study enrolling at least 240 and up to 250 randomized subjects at up to 45 study centers across the U.S. Enrollment will be conducted in 2 consecutive stages:

- Stage 1 with 60 randomized subjects at up to 25 study centers; and
- Stage 2 with approximately 190 randomized subjects at up to 45 study centers, including those from Stage 1.

There will be a pause in enrollment after enrollment in Stage 1 is completed. This pause in enrollment is intended to allow completion of Week 12 assessments by 60 enrolled and randomized subjects and an interim analysis (see Section **4.2**). The primary analysis will occur after the last enrolled and randomized subject in Stage 2 completes Week 12 assessments, which is defined as the last subject's Week 12 visit (see Section **4.3**).

After completing primary endpoint assessments at Week 12, there will be a one-way crossover of control subjects to active stimulation and a 252-week open-label follow-up with all subjects receiving active stimulation to evaluate long-term safety. Blinding will be maintained until the last enrolled and randomized subject in Stage 2 completes Week 12 assessments, and the study dataset for the primary analysis is locked.

3.3 Study Visits and Assessments

On the same day that written consent is obtained, each subject will undergo physical examination, RA disease activity assessments and review of prior and current RA medications to confirm their initial eligibility and baseline values for the primary and key secondary efficacy endpoints. The

remaining screening assessments, including blood work and pre-surgical clearance, will be completed prior to Implant Procedure, which shall be performed within 30 days from informed consent. Post-Surgical Clearance will be performed between 14 and 21 days from Implant Procedure. Day 0 assessments, randomization and initial device titration will be performed after completing Post-Surgical Clearance and within 14-21 days from Implant Procedure. There will be 3 additional device titration visits (Titration 1, 2, 3 at Week 1, 2 and 3, respectively), 3 follow-up RA assessment visits (Week 4, 8, 12 primary efficacy endpoint and a one-way crossover) as detailed in Schedule of Assessments (see **Appendix A**).

During open-label, long-term follow-up there will be 3 device titration visits (Titration 4, 5, 6 at Week 13, 14, 15, respectively), and 21 follow-up RA assessment visits every 12 weeks from Week 24 through Week 264 (end of study) as detailed in CLP-001.

3.4 Sample Size and Power

The sample size is calculated based on an estimated 60% response rate at Week 12 in the treatment group and 30% response rate at Week 12 in the control group. A sample size of 250 randomized subjects, 125 in each group, offers 96% power to detect a difference of 30% at the one-sided alpha of 0.025. If the true response rates are 50% in the treatment and 30% in the control group, the sample size of 250 subjects has 77% power to detect a difference of 20% at the one-sided alpha of 0.025. The table below provides additional power calculations for 250 subjects using estimated response rates of 20 to 40% in control and 35-70% in treatment (**Table 1**). The table also shows power if enrollment ends at 240 subjects. The decrease in power is <1% for all scenarios and most often <0.5%.

Table 1: Power Calculation Based on Estimated ACR Response Rate

Control (%)	Treatment (%)	Difference (%)	Power N = 250	Power N=240
20	50	30	0.967	0.966
20	45	25	0.917	0.916
20	40	20	0.812	0.807
20	35	15	0.609	0.601
30	60	30	0.959	0.959
30	55	25	0.900	0.898
30	50	20	0.773	0.770
30	45	15	0.555	0.549
40	70	30	0.959	0.958
40	65	25	0.897	0.893
40	60	20	0.762	0.750

All p-values are one-sided based on the chi-square test stratified incomplete response to JAKi and include futility stopping. Power based upon 1,000,000 simulations per scenario.

The smallest statistically significant difference that can be detected in the sample of 250 randomized subjects ranges from 11.2% to 12.8% for control rates of 20% to 40%, respectively.

4 TYPE OF PLANNED ANALYSIS

4.1 DMC Analysis

An independent Data Monitoring Committee (DMC) consisting of external, independent rheumatology, surgery and biostatistics experts will be assessing the safety and efficacy of the interventions during the trial and perform ongoing monitoring of overall study conduct. The DMC's role and responsibilities and the scope of study oversight are detailed in the DMC Charter, which defines the DMC membership, meeting logistics, and meeting frequency.

After initiation of the study, the DMC will meet regularly (i.e., after enrollment of every 15 subjects through Stage 1 and once every three months from the start of Stage 2 until the last study subject has been enrolled, and then once every six months after completing Stage 2 enrollment through Week 264. In accordance with the DMC Charter, the DMC will provide recommendations for continuing or stopping the study based on their ongoing review of cumulative safety data, including reasons for screening failure, subject disposition, AEs, SAEs, device deficiencies, protocol deviations, and concomitant medications, as well as descriptive summaries of TJC28 and SJC28. At the end of Stage 1, the DMC will review the outcomes of a formal interim analysis (see Section **4.2**). Closed Sessions will occur until the study is unblinded after data lock and primary analysis.

4.2 Interim Analysis

One formal interim analysis is planned at the end of Stage 1 when approximately 60 randomized subjects have reached their Week 12 endpoints. The purpose of this interim analysis is to check for safety risks and a lack of efficacy prior to commencing enrollment for Stage 2. No early success stopping may possibly occur. Therefore, there is no alpha-spending as there is no possibility for early claim. As these data contribute to the overall device experience for the safety review, and no early success stopping is permissible, no Type I error inflation occurs with such interims.

4.2.1 Stopping rule

The DMC and FDA will review the 12-week unblinded data from Stage 1, including demographics, efficacy, safety, enrollment rates, and device implantation rates, and determine whether the following stopping rule is met:

- The observed difference between treatment and control in the proportion of subjects achieving the ACR20 response at Week 12 from baseline on the day of informed consent is less than 10%.

This stopping rule in 60 subjects balances the need to stop a trial with a projected low probability of success with a need to avoid prematurely stopping a potentially successful trial after Stage 1, given the decision is based on a dichotomous endpoint in a relatively small number of subjects.

For illustrative purposes, the table below provides stopping probabilities for 60 randomized subjects and their effect on power in 250 randomized subjects, using an estimated ACR20 response rate of 30% in the control group and a range of 35-60% in the treatment group (**Table 2**). The proposed rule has a 50% probability of stopping a study having < 30% power to meet the primary efficacy objective in 250 subjects. Type 1 error is maintained at 2.5% even without the futility stop. The last column in the table shows power if enrollment ends at 240 subjects. Again, the power decreases by < 1% in all scenarios.

Table 2: True Probability of Stopping after Stage 1 and Power of Study Success Based on Pooled Data

Control	Treatment	Probability of Stopping N = 60 (Stage 1)	Power N = 250 (Stage 1 + 2)	Power N = 240 (Stage 1 + 2)
30%	60%	0.040	0.959	0.959
30%	55%	0.089	0.900	0.898
30%	50%	0.173	0.773	0.770
30%	45%	0.293	0.555	0.549
30%	40%	0.444	0.291	0.282
30%	35%	0.608	0.096	0.093
30%	30%	0.760	0.017	0.017

Operating characteristics calculated by simulating 1,000,000 trials per scenario using chi-square test.

4.2.2 Communication plan

The Stage 1 efficacy and safety data for all 60 enrolled and randomized subjects will be exported from the database and directly delivered to an independent, non-voting, biostatistician who will analyze the data and report to the DMC without any involvement from the sponsor and study biostatisticians (**Table 3**). The independent biostatistician will analyze the data by randomization group, create an interim report and submit the report with the datasets, programs and program outputs to the DMC. The interim report will be reviewed by the DMC in a Closed Session. The DMC Chairperson will convey whether or not the stopping rule is triggered to the Chief Executive Officer (CEO) of SetPoint Medical.

If the stopping rule is triggered, the CEO or designee will notify the FDA about the DMC's decision and the study will be terminated. The study will be unblinded, and all Stage 1 data analyzed. The sponsor will submit to the FDA a report with the DMC's decision together with the datasets, programs and program outputs as well as any proposals for further clinical research.

If the stopping rule is not triggered, the sponsor will initiate an IDE Supplement to the FDA to request commencement of Stage 2 enrollment, and will provide the name and contact information

of the statistician from whom the FDA will request the Interim Report containing unblinded data. The unblinded data will be provided directly to the FDA upon request, maintaining blinding of the sponsor. The study will advance to Stage 2 only after receiving approval from the FDA.

The DMC Chairperson may also convey to the CEO the point estimates for ACR20 response rate in the treatment and control groups, if requested by the Board of Directors or potential key investors as a contingency for financing of Stage 2. The request and response will be documented and not shared with anyone directly or indirectly involved in the management of the study. The access to and communication of the interim findings will be tightly controlled to mitigate the introduction of operational bias and documented in reports submitted by the CEO to the DMC Chairperson following the communication procedures detailed in the DMC Charter.

Table 3: Interim Data Access Matrix

Department/Role	Blinded	Unblinded	Note
CEO	B	--	Receiving DMC's recommendations and decision as yes or no on the Stage 1 stopping rule and point estimates if requested by the board or investors as a contingency for financing Stage 2
Clinical Operations[1]	B	--	Not having access to randomization assignments or DMC Closed Session reports to preserve blinding of everyone involved directly or indirectly in the study conduct until locking the study dataset for the primary efficacy analysis at Week 12
Clinical Data Management	B	--	Consultants to sponsor responsible for managing EDC and IRT, generating blinded data exports and not having access to randomization assignments until locking the study dataset for the primary efficacy analysis at Week 12
Study Biostatisticians	B	--	Consultants to sponsor responsible for programming but not having access to randomization assignments until locking the study dataset for the primary efficacy analysis at Week 12
Independent Biostatistician	--	U	Non-voting statistician reporting to DMC responsible for receiving blinded data exports, accessing randomization assignments, conducting unblinded analyses and preparing outputs for review during DMC closed sessions
DMC	--	U	DMC chairperson, biostatistician, and clinicians participating in closed meetings

Abbreviations: B, blinded; CMO, Chief Medical Officer; CRA, clinical research associates; DMC, data monitoring committee; EDC, electronic data capture; IRT, Interactive response technology; U, unblinded;.

[1]Clinical operations includes, but is not limited to, Chief Medical Officer, Vice President of Clinical Affairs, Managers of Clinical Affairs/Operations, Clinical Research Associates, Field Clinical Engineers

4.3 Primary Analysis

After the last enrolled and randomized subject in Stage 2 has completed all Week 12 assessments or been lost to follow-up, all outstanding data queries related to primary analysis have been resolved or determined to be unresolvable, and the data have been cleaned, finalized and locked, the study blind will be broken, and the primary analysis of the efficacy and safety data will be performed. The primary analysis at Week 12 will include all population analyses and endpoints using pooled data from all subjects enrolled and randomized in Stage 1 and 2 (**Table 4**: Summary of Primary and Secondary Efficacy Endpoints at Week 12).

Table 4: Summary of Primary and Secondary Efficacy Endpoints at Week 12

Endpoint	Display	ITT	PTE	Sensitivity	Subgroup	Missing Data Imputation
Primary						
ACR20 response	T, L	Y	Y	Y [1]	Y	NRI
Key Secondary Adjusted for Multiplicity						
ACR20 response from Day 0	T, L	Y	Y	Y [1]	Y	NRI
DAS28-CRP good/moderate EULAR response	T, L	Y	Y	Y [2]	Y	NRI
DAS28-CRP response (MCID)	T, L	Y	Y	Y [2]	Y	NRI
HAQ-DI response (MCID)	T, L	Y	Y	Y [2]	Y	NRI
Exploratory Secondary [3]						
ACR50/70 response	T, L	Y	--	--	--	--
ACR Components (TJC28, SJC28, Subject Pain, SGA, EGA, HAQ-DI, hsCRP) 20/50/70 response	T, L	Y	--	--	--	--
Mean HAQ-DI score change at Week 12	T, L	Y	--	--	--	--
DAS28-CRP score change, LDA/remission	T, L	Y	--	--	--	--
CDAI score change, LDA/remission, response	T, L	Y	--	--	--	--
SF-36/PCS/MCS score change	T, L	Y	--	--	--	--
EQ-5D-5L score change	T, L	Y	--	--	--	--
RAMRIS (bone erosion, osteitis, synovitis, CARLOS) score change, progression (bone erosion)	T, L	Y	--	--	-	--
Percent change in plasma biomarkers	T, L	Y	--	--	--	--
BI for subject's blinding assessment	T, L	Y	Y	--	--	--
BI for Joint Evaluator's blinding assessment	T, L	Y	Y	--	--	--
BI for Co-PI Rheumatologist's blinding assessment	T, L	Y	Y	--	--	--

Abbreviations: ACR, American College of Rheumatology; BI, Bang's blinding index; CARLOS, cartilage loss score; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS, Disease Activity Score; EGA, evaluator's global assessment; EQ-5D-5L, EuroQol 5 domains 5 levels; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high sensitivity CRP; ITT, intent to treat; L, listings; LDA, low disease activity; NRI, non-responder imputation; PTE, per treatment evaluable; RAMRIS, Rheumatoid Arthritis MRI Scoring System; SF-36, Short Form Survey with 36 items; SGA, subject's global assessment; T, tables; TJC, tender joint count; SJC, swollen joint count; Y, yes.

Note: All response rates are at Week 12 based on change from baseline, unless stated otherwise. Refer to Section **8.1** for definitions of missing data imputation strategies. Refer to Sections **8.2**, **8.3**, **8.4** and **8.6** for definition of response for specific endpoints. All score values are determined at all timepoints and for change from baseline.

[1] Sensitivity analyses for rescue treatments and missing data.
[2] Sensitivity analysis for timing of baseline, rescue treatments and missing data.
[3] Approaches to handling of missing data are given in Section **8.1**

5 STATISTICAL METHODS

5.1 General Considerations for Data Analyses

The primary efficacy endpoint, all secondary efficacy endpoints, exploratory analyses identified here, and safety evaluations are considered *a priori* analyses because they have been prespecified in the SAP prior to locking the dataset and reviewing unblinded results. All other analyses, if any, designed subsequent to locking the dataset will be considered *post-hoc* analyses, and their results will be considered exploratory. Any *post hoc* analyses will be clearly identified in the clinical study report.

Continuous data will be summarized in terms of the mean, SD, median, minimum, maximum and number of observations, unless otherwise stated. The minimum and maximum will be reported to the same number of decimal places as the raw data recorded in the database. The mean and median will be reported to 1 more decimal place than the raw data recorded in the database. The SD will be reported to 2 more decimal places than the raw data recorded in the database. In general, the maximum number of decimal places reported shall be 4 for any summary statistic.

Categorical data will be summarized in terms of the number of subjects providing data at the relevant time point, frequency counts and percentages. If not stated otherwise, percentages will be presented with one decimal place. Percentages will not be presented for zero counts. Percentages will be calculated using n as the denominator. 100% will be presented without decimal places.

P-values greater than or equal to 0.001, in general, will be presented to 3 decimal places. P-values less than 0.001 will be presented as "< 0.001".

95% Confidence intervals (CI) will be presented to 1 more decimal place than the raw data. Unless stated otherwise, a two-sided 95% confidence level will be calculated when confidence interval is presented.

Data from the protocol-specified visits (i.e., as reported in CRF) will be used in the summary tables (**Appendix B**) and data listings (**Appendix C**). All report outputs will be produced using a software package widely recognized as acceptable for analyzing clinical data in a secure and validated environment.

The analyses for the primary and secondary efficacy endpoints are detailed below:

- The primary ACR20 response at Week 12 will be analyzed with the Cochran-Mantel-Haenszel (CMH) test. For Stage 1 subjects, stratification factors are prior inadequate response or loss of response to JAKi and RA disease severity of < 4 TJC28 or < 4 SJC28 at Day 0. For Stage 2 subjects, stratification factors are RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action. Other binary response endpoints at Week 12 will be analyzed similarly.
- The secondary efficacy endpoints that are continuous variables (change from baseline) will be analyzed using Mixed-effect Model Repeated Measure (MMRM) statistics. The repeated-measures analysis will be based on the restricted maximum likelihood method assuming an unstructured covariance structure to model the within-subject errors. The model, including:

treatment group; stratification factors - inadequate response or loss of response to JAKi and RA disease severity at Day 0 (Stage 1 subjects); RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action (Stage 2 subjects); visit (all visits from Week 4 to Week 12); and treatment-by-visit interaction as fixed effects and baseline as a covariate, will be used to test the difference between the treatment and control group in a given efficacy endpoint change from baseline to Week 12. The data collected after receiving rescue therapy will be set to missing. Therefore, the MMRM analysis assumes a missing-at-random (MAR) mechanism for missing data due to dropout and post-rescue data.

5.2 Analysis Populations

Analysis population defines the subjects to be included in an analysis. The primary efficacy analyses for the primary and key secondary endpoints will be conducted on the intent-to-treat (ITT) and per-treatment-evaluable (PTE) populations. The exploratory analyses will be conducted on the ITT population as detailed in **Table 4**. All analysis populations are defined below:

- *ITT population*. All enrolled and randomized subjects in Stage 1 and 2.
- *PTE population*. Subjects from ITT population who have received the assigned treatment, who have no major procedural protocol deviations (see Section **9.2**) and for whom follow-up data are available.
- *Safety population*. All enrolled subjects in Stage 1 and 2.

5.3 Baseline

Information and RA disease activity assessments collected during Screening on the day of informed consent will be used to confirm initial eligibility and as the baseline assessments for determination of the primary and key secondary efficacy endpoints (**Table 5**).

Baseline assessments for the exploratory endpoints (e.g., EQ-5D-5L, SF-36, RAMRIS, biomarkers) will be collected during Screening.

Table 5: RA Disease Activity Assessments to Be Collected on the Day of Informed Consent and Used as the Baseline Assessments for Determination of the Primary and Key Secondary Efficacy Endpoints

Endpoint	HAQ-DI	SGA	Subject Pain	TJC28	SJC28	EGA	hsCRP
Primary							
ACR20 response	Y	Y	Y	Y	Y	Y	Y
Key Secondary Adjusted for Multiplicity							
ACR20 response from Day 0	Y	Y	Y	Y	Y	Y	Y
DAS28-CRP good/moderate EULAR response	--	Y	--	Y	Y	--	Y
DAS28-CRP response (MCID)	--	Y	--	Y	Y	--	Y
HAQ-DI response (MCID)	Y	–	--	–	--	–	--

Abbreviations: ACR, American College of Rheumatology; CRP, C-reactive protein; DAS, Disease Activity Score; EGA, evaluator's global assessment; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high sensitivity CRP; SGA, subject's global assessment; TJC, tender joint count; SJC, swollen joint count; Y, yes.
Note: All response rates are at Week 12 based on change from baseline at the time of informed consent, unless stated otherwise.

5.4 Study Day Calculation

Study day is calculated relative to the date of Day 0 (randomization) and will appear in the listings where applicable. If the date of event is on or after Day 0, study day will be calculated as:

Study day = date of event – date of Day 0 (randomization)

5.5 Randomization

After completing the protocol-required assessments at Day 0, all enrolled subjects (i.e., meeting all the inclusion and none of the exclusion criteria in whom the implant procedure was attempted) that were implanted will be assigned in a 1:1 ratio to either the treatment or the control group. The randomization scheme will be generated by the study biostatisticians and implemented centrally through Interactive Response Technology (IRT).

The randomization will be stratified to help ensure balanced distribution between treatment groups. For Stage 1 subjects, stratification factors are inadequate response or loss of response to JAKi and RA disease severity of < 4 TJC28 or < 4 SJC28 at Day 0. For Stage 2 subjects, stratification factors are RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action.

Enrollment will continue until at least 240 and up to 250 subjects are randomized. If there are discrepancies in stratification factor values between the IRT and EDC systems, the data recorded in the EDC will be used for analyses.

5.6 Change from Baseline Calculation

Percent change from baseline to any time point (e.g., Day 0, Week 4, 8 or 12) will be calculated as follows:

$$[\text{Value}_{(\text{Post-baseline})} - \text{Value}_{(\text{Baseline})}] / \text{Value}_{(\text{Baseline})} \times 100$$

A negative value reflects a decrease in a given parameter, while a positive relative difference reflects an increase in the parameter.

5.7 Relative Difference Calculation

Relative difference between treatment and control groups at any time point will be calculated as:

$$[\text{Value}_t - \text{Value}_c] / \text{Value}_c \times 100$$

A negative relative difference reflects a decrease in a given parameter on the treatment side compared to control, while a positive relative difference reflects an increase in the parameter on the treatment side compared to control.

5.8 Missing Dates

In analysis of AEs and medication, a complete date will be established in order to identify AEs or medication as occurring during treatment or not. For handling partially reported onset/start and outcome/end dates for AEs or medication the following algorithms are applied:

- AEs:
  - Missing onset day, but month and year present:
    - If baseline visit occurred in the same month and year as the occurrence of the AE, then the onset day of the event is assigned to the date of baseline visit.
    - Otherwise, the onset day is set to the first day of the month (e.g., XX-Sep-2020 is considered as 01-Sep-2020).
  - Missing onset day and month, but year present:
    - If baseline visit occurred in the same year as the occurrence of the AE, then the onset date of the event is assigned to the date of baseline visit.
    - Otherwise, the onset day and month is set to 01 January (e.g., XX-XXX-2020 is considered as 01-Jan-2020).
  - Missing outcome day, but month and year present:
    - The day is set to the last day of the month (e.g., XX-Sep-2020 is considered as 30-Sep-2020).
  - Missing outcome day and month, but year present:
    - The outcome day and month is set to 31 December (e.g., XX-XXX-2020 is considered as 31-Dec-2020).
- Medications:
  - Missing start day, but month and year present:
    - If baseline visit occurred in the same month and year as the occurrence of the medication, then the start day of the medication is assigned to the date of baseline visit. Otherwise, the start day is set to the first day of the month (e.g., XX-Sep-2020 is considered as 01-Sep-2020).
  - Missing start day and month, but year present:
    - If baseline visit occurred in the same month in the same year as the occurrence of the medication, then the start date of the medication is assigned to the date of baseline visit.
    - Otherwise, the start day and month is set to 01 January (e.g., XX-XXX-2020 is considered as 01-Jan-2020).
  - Missing stop day, but month and year present:
    - The day is set to the last day of the month (e.g., XX-Sep-2020 is considered as 30-Sep-2020).
  - Missing stop day and month, but year present:

    - The stop day and month is set to 31 December (e.g., XX-XXX-2020 is considered as 31-Dec-2020).

- Date of RA diagnosis:
  - Missing day, but month and year present:
    - Date is set to the first day of the month (e.g., XX-Sep-2010 is considered as 01-Sep-2010).
  - Missing day and month, but year present:
    - Date is set to 01 January (e.g., XX-XXX-2010 is considered as 01-Jan-2010)
- Week 12 visit:
  - If the Week 12 visit date is missing (e.g., the subject missed the Week 12 assessment but is still participating in the study), the Week 12 visit date will be set to the date that subject's MicroRegulator was re-registered for open-label, long-term follow-up

5.8.1 Missing data for efficacy and safety endpoints

Missing data for each efficacy endpoint will be handled as described in Sections 8.2, 8.3, 8.4 and 8.6.

For continuous endpoints, change from baseline will be set to missing at visits with missing post-baseline values or where data were imputed to missing. Continuous efficacy endpoints will be set to missing for subjects who received rescue treatment before Week 12.

For binary endpoints, subjects with missing efficacy data, early withdrawals, or subjects who received rescue treatment before Week 12 will be imputed as non-responders and therefore treated as a failure (e.g., no ACR20/50/70 response, DAS28-CRP remission or no moderate/good EULAR response).

Additional rules for handling of missing data and rescue treatments are detailed below:

- *Missing efficacy data*. Visits with missing data (due to a missed visit or missing component of a composite endpoint) will be set to treatment failure.
- *Early withdrawals*. Only visits following the early withdrawal visit will be set to treatment failure.
- *Prednisone equivalent >10 mg/day*. The visit after a period (time from previous visit up to the day before the current visit) of average daily corticosteroid use exceeding 10 mg/day prednisone will be set to treatment failure and continuous endpoints set to missing due to rescue.
- *Corticosteroid injection*. If subject received a corticosteroid injection within 30 days prior to a study visit, that visit will be set to treatment failure and continuous endpoints set to missing due to rescue.
- *b/ts/csDMARD*. Subjects who receive treatment before Week 12 with biologic, targeted synthetic, or additional conventional synthetic DMARD, or increased dose of background

conventional synthetic DMARD will be set to treatment failure at all subsequent visits and continuous endpoints set to missing due to rescue.

- *Missing baseline value.* For efficacy endpoints, a missing value at baseline will not be imputed, and the endpoint will be set to missing for all visits.
- *Missing analytes/ retests*. If an analyte value is missing/its concentration cannot be reliably determined (e.g., sample was lost, damaged, etc.), a retest value will be used for that analyte. If an initial value is non-missing and reliable but the analyte was retested, the value that coincides with the date of clinical assessment will be used. If neither an initial nor retest value is available, the analyte value will be set to missing.

5.8.2 Multiple Assessments and Visits

If a variable (e.g., MRI, TJC, SJC) has been assessed multiple times at the same visit, only the last assessment will be used.

Only completed scheduled visits will be included in summary tables (**Appendix B**). Listings will include scheduled and unscheduled visits (**Appendix C**).

5.9 Data Assurance

All tables, figures and data listings to be included in the report will be independently checked for consistency, integrity and in accordance with the study sponsor's SOPs.

5.10 Consistency Across Study Centers

The consistency of ACR 20 response rate across the study centers will be evaluated using Breslow Day test for homogeneity. Any center with < 5 subjects with ACR20 data in any treatment group will be pooled from largest to smallest until the pooled center has 5 subjects in each treatment group. If heterogeneity is found, exploratory analysis will be conducted to investigate the issue. This may include analysis adjusted for baseline characteristics that significantly differ across sites.

5.11 Coding Dictionaries

AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 21.0 or later). Concomitant medications will be coded using the March 2019 or later version of the WHO Drug Global dictionary.

6 SUBJECT DISPOSITION

6.1 Subject Enrollment and Disposition

A summary of subject enrollment will be provided by treatment group for each site. The summary will present the number and percentage of subjects enrolled. For each column, the denominator for the percentage calculation will be the total number of subjects analyzed for that column.

A similar enrollment table will be provided by stratification factor stratum. The denominator for the percentage of subjects in the stratum will be the total number of enrolled subjects. If there are discrepancies in the value used for stratification assignment between the IRT and EDC systems, the value collected in the EDC will be used for the summary.

A listing of subjects with discrepancies in the value used for stratification assignment between the IRT and EDC systems at the time of data finalization will be provided.

The randomization schedule used for the study will be provided in a listing and as an appendix to CSR.

The number and percentage of subjects in whom the implant procedure was attempted and in whom it was successful will be summarized. The primary reason for subject discontinuation will be summarized. Screen failures will be reported in the data listings and the summary table. Data for subject disposition, including termination date and reason, will be listed.

7 DEMOGRAPHICS AND BASELINE CLINICAL CHARACTERISTICS

Demographic data (i.e., age, gender, race, ethnicity) and baseline clinical characteristics (i.e., years since RA diagnosis, treatment history with biologic, targeted synthetic and conventional synthetic DMARDs, baseline clinical variables) will be summarized per treatment group and overall using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables.

8 EFFICACY ANALYSES

8.1 General Considerations

8.1.1 Missing endpoint data imputation

Below are the descriptions for the imputation methods that may be used throughout the efficacy analyses:

- *Observed case (OC).* Missing values remain missing. For the categorical composite endpoints, in the case that some components are missing, the composite endpoint assessment will be derived based on the non-missing components. If non-missing components are not sufficient to determine final composite endpoint, then the composite endpoint will be set as missing. For continuous composite endpoints, if any components are missing, the composite endpoints will be set as missing.
- *Last observation carried forward (LOCF).* Baseline and Day 0 measurements will not be carried forward to post-baseline. Only measurements post Day 0 will be LOCF for continuous and binary response measures. For the composite endpoints, the last non-missing, post-Day 0 observation will be carried forward to subsequent visits for each individual component first, and then the composite endpoints using individual components imputed by LOCF will be calculated as described above. If a subject does not have a non-missing observed record for a post-Day 0 visit, the last post-Day 0 record prior to the missed visit will be used. If the last non-missing observation prior to the missing visits cannot be determined due to multiple

measurements occurring at the same time or the time not available within the same day, the worst outcome will be used for LOCF. If missing components still exist after LOCF, the composite endpoints will be calculated using the same rules as described in OC.

- *Non-responder imputation (NRI)*. For all binary response measurements, starting from OC, all missing will be set as non-responders.

If subject only had baseline measurements, LOCF and OC analyses will not include this subject. But this subject will be treated as non-responder in NRI analyses.

8.2 Clinical Variables

8.2.1 TJC28 and SJC28

The assessment for swelling is the total number of joints with a present swelling and ranges from 0 to 28 for SJC28. The assessment for tenderness is the total number of joints with a present tenderness and ranges from 0 to 28 for TJC28. The following 28 joints will be taken into account for TJC28 and SJC28: shoulder (2 joints), knee (2), elbow (2), wrist (2), fingers (PIP, MCP: 20). All joint assessments will be performed by an independent, blinded joint evaluator. Artificial, ankylosed and missing joints are excluded from swelling and tenderness assessment.

If there are missing observations for tender or swollen joints, then the remaining observations will be assessed and weighted by dividing the number presented by number of non-missing and by multiplying by 28 for the joint count. No imputations for individual joints will be done. If a joint is not evaluable at baseline, then that joint is set to missing throughout the study. If data for more than 50% of the joints are missing at the time of a given assessment, then the total count will be set to missing for that visit.

8.2.2 SGA

Subjects will complete a global assessment of their RA disease activity using the subject's global assessment of disease activity (SGA) item, a numerical rating scale (NRS) from "0" (inactive) to "10" (very active).

No imputations for missing data will be done.

8.2.3 Subject's Pain Assessment

Subjects will assess the severity of their current RA-related pain using a NRS from "0" (no pain) to "10" (worst pain imaginable).

No imputations for missing data will be done.

8.2.4 EGA

The joint evaluator will complete the evaluator's global assessment of disease activity item (EGA) using a NRS from "0" (inactive) to "10" (very active).

No imputations for missing data will be done.

8.2.5 HAQ-DI

The functional status of the subject will be assessed by means of the Health Assessment Questionnaire Disability Index (HAQ-DI). This 20-question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas:

- Dressing and grooming
- Arising
- Eating
- Walking
- Hygiene
- Reach
- Grip
- Common daily activities

Each functional area contains at least 2 questions. For each question, there is a 4-level response set that is scored from 0 (without any difficulty) to 3 (unable to do). If aids or devices or physical assistance are used for a specific functional area (**Table 6**), and the maximum response of this functional area is 0 or 1, the according value is increased to a score of 2.

Table 6: HAQ-DI Category Scores Depending on Aids, Devices or Physical Assistance

Aid or Equipment	Will be Associated with Category Score
Walking stick/frame, crutches, wheelchair	Walking
Aids used for dressing	Dressing and grooming
Specially adapted utensils	Eating
Specially adapted chair	Rising
Raised toilet seat, bath rail, bath seat	Hygiene
Long-handled appliance in bathroom	Hygiene
Long-handled appliance for reaching	Reach
Jar opener	Grip
Other (1)	Dressing & grooming, rising, eating, walking
Other (2)	hygiene, reach, grip, common daily activities

If "other" is marked as an aid or equipment, then this can be assigned to a group of four functional areas and will be handled as an aid or equipment for each of the four functional areas. Therefore,

if the maximum score of a functional area is 0 or 1, that value is increased to a score of 2 for each of the four functional areas.

Regarding these corrections, the highest response within each functional area determines the score of that specific functional area. If no questions within a given functional area were answered, no score will be provided for that category (even if answers on aids or equipment are available).

HAQ-DI score is only calculated if there are at least 6 functional area scores available. The average of these non-missing functional area scores defines the continuous HAQ-DI score ranging from 0 to 3. If there are less than 6 functional area scores available, no imputation will be done, and the HAQ-DI will be set to missing for the corresponding assessment.

A HAQ-DI score reduction from baseline by 0.22 represents the MCID.

8.2.6 hsCRP

Blood concentration of hsCRP (mg/L) for all subjects will be determined by a central laboratory.

8.3 Primary Efficacy Endpoint

- ACR20 response at Week 12

8.3.1 Definition

A subject achieves ACR20 response when this subject experiences a $\geq$ 20% improvement from baseline on the day of informed consent to Week 12 in TJC28, SJC28, and at least 3 of the following 5 items:

- Subject's pain assessment
- SGA
- EGA
- HAQ-DI
- hsCRP

For all visits, if any of the component scores are missing, then those scores will be considered as not having met the criteria for improvement. If 3 or more of the 5 remaining ACR measures are missing, ACR20 will each be considered as "no response" in the final dataset.

For component scores with missing baseline values or a baseline value of 0, the percentage improvement cannot be calculated, and the component will be considered as not having met the criteria for improvement for all visits.

8.3.2 Statistical Hypothesis

The hypothesis of interest is:

H_0: $p_t - p_c = 0$

H_1: $p_t - p_c > 0$

where p_t is the response rate in the treatment group and p_c is the response rate in the control group. The study will test the null hypothesis (H_0) that there is no difference between the treatment and control groups in the proportion of subjects achieving ACR20 response at Week 12 versus the alternative hypothesis (H_1) that treatment group response rate exceeds the control group response rate. The study will be considered successful if there is a statistically significant improvement in the proportion of subjects with ACR20 response in favor of the SetPoint System at the one-sided alpha of 0.025.

8.3.3 Primary Analysis

The primary analysis of the ITT population will be the CMH test. ACR20 response is the outcome variable. Subjects who received rescue treatment before Week 12 or who had missing data at Week 12 will be considered non-responders in the primary analysis.

8.3.4 Sensitivity Analyses

Sensitivity analysis for rescue intervention

Because rescue interventions can potentially confound the primary efficacy outcome, a sensitivity analysis will be performed to test the robustness of the efficacy conclusion to actual interventions given.

In this analysis, data imputations will be performed if intervention is given prior to Week 12, then ACR20 value prior to the intervention will be used in the analysis (LOCF).

Sensitivity analysis for missing data

Subjects with missed visit, lost to follow-up or partial ACR20 will be considered as missing data. If more than 5% of the primary efficacy data are missing, the following imputation analyses will be performed to assess the sensitivity of conclusions to missing data:

- A "tipping point" analysis in which all the primary analysis will be performed with all combinations of missing data. For instance, with M_C subjects with missing Week 12 data in the control group and M_t subjects with missing Week 12 data in the treatment group, then all Mc × Mt possible interims are completed. Between-treatment comparisons will be performed using a chi-squared test for each possible combinations of J (from 0 to Mc) and K (from 0 to Mt). The tipping point analysis will include the following cases:
  - Impute "ACR20 responder" for all missing values in the control group and "ACR20 non-responder" in the treatment group; this is a worst-case imputation.
  - Impute "ACR20 non-responder" for all missing values in the control group and "ACR20 responder" in the treatment group; this is a best-case imputation.

- If the decision about the null hypothesis using worst-case imputation agrees with the decision about the null hypothesis using best-case imputation, the tipping point analysis will include no further cases.

- In addition, an analysis will be conducted in which ACR20 responder or non-responder will be imputed based upon the last observed value (at Week 8 or Week 4) according to fully conditional specification predictive mean matching multiple imputation approach of Berglund and Heeringa (2014).

8.3.5 Subgroup Analyses

The primary efficacy endpoint will be examined using the following subgroups (including but not limited to the ones listed below):

- Age (< 65 vs. ≥ 65)
- Gender (male vs. female)
- Race (White vs. Non-White, including Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander)
- Duration of RA (< 5 years vs. ≥ 5 to < 10 years vs. ≥ 10 years)
- Number of prior biologic and targeted synthetic DMARDs (e.g., < 4 vs. ≥ 4)
- Prior use of JAKi (Yes vs. No)
- RA disease activity at Screening (DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1)
- Moderate-to-severe RA at Day 0 (< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28)

8.4 Key Secondary Endpoints

- ACR20 response at Week 12 from Day 0
- DAS28-CRP good/moderate EULAR response at Week 12 from baseline
- DAS28-CRP response (MCID -1.2) at Week 12 from baseline
- HAQ-DI response (MCID -0.22) at Week 12 from baseline

8.4.1 Definitions of key secondary endpoints

ACR20 response at Week 12 from Day 0

A subject achieves ACR20 response when this subject experiences a ≥ 20% improvement at Week 12 from the post-surgical baseline at Day 0 in TJC28 and SJC28 and 3 out of 5 ACR core measures and follows the same general and statistical analyses as for ACR20 response at Week 12 from baseline on the day of informed consent (see Section **8.3.1**).

DAS28-CRP good/moderate EULAR response at Week 12

DAS28-CRP EULAR response at Week 12 is defined based on the combination of the current DAS28-CRP score and its improvement relative to baseline on the day of inform consent as illustrated in **Table 7**.

Table 7: EULAR Response Criteria

DAS28-CRP Score Week 12	DAS28-CRP Score Decrease from Baseline Value		
	> 1.2	**> 0.6 to ≤ 1.2**	**≤ 0.6**
≤ 3.2	Good response	Moderate response	No response
> 3.2 to ≤ 5.1	Moderate response	Moderate response	No response
> 5.1	Moderate response	No response	No response

A subject is considered having a moderate treatment response at Week 12 if:

- DAS28-CRP score improvement from baseline to Week 12 is > 0.6 and ≤ 1.2, and the DAS28-CRP score at Week 12 is ≤ 5.1; or
- DAS28-CRP score improvement from baseline to Week 12 is > 1.2, and the DAS28-CRP score at Week 12 is > 3.2.

A subject is considered having a good treatment response at Week 12 if:

- DAS28-CRP score improvement from baseline to Week 12 is > 1.2 and the DAS28-CRP score at Week 12 is ≤ 3.2.

If the post-baseline DAS28-CRP score is missing, then the corresponding EULAR category will be missing.

Missing DAS28-CRP values will be considered as not achieving remission.

DAS28-CRP response (MCID -1.2) at Week 12

A DAS28-CRP score reduction by at least 1.2 from baseline on the day of inform consent to Week 12 represents the MCID response (see Section **8.6.1**).

HAQ-DI response (MCID -0.22) at Week 12

A HAQ-DI score reduction by at least 0.22 from baseline on the day of inform consent to Week 12 represents the MCID response (see Section **8.2.5**).

8.5 Multiplicity Adjustment of Key Secondary Endpoints

This section describes the methods that will be used to control the familywise type 1 error rate (FWER) among these 4 secondary endpoints. If and only if the primary efficacy objective is met,

the Hochberg's step-up procedure (Hochberg 1988) will be used to control the FWER at a 1-sided significance level of 0.025 for the following 4 secondary endpoints:

ACR20 response at Week 12 from Day 0

- Test: H_0: pt - pc = 0 H_1: pt - pc > 0, using stratified CMH test, as detailed in Section **5.1**

DAS28-CRP good/moderate EULAR response at Week 12 from baseline on the day of informed consent

- Test: H_0: pt - pc = 0 H_1: pt - pc > 0, using stratified CMH test

DAS28-CRP response (MCID -1.2) at Week 12 from baseline on the day of informed consent

- Test: H_0: pt - pc = 0 H_1: pt - pc > 0, using stratified CMH test

HAQ-DI response (MCID -0.22) at Week 12 from baseline on the day of informed consent

- Test: H_0: pt - pc = 0 H_1: pt - pc > 0, using stratified CMH test

The procedures rank the p-values from the above 4 tests from the least significant and examines the other p-values in a sequential manner until it reaches the most significant one, i.e., p(4) > p(3) > p(2) > p(1).

The decision rule for the Hochberg procedure is defined as follows:

- Step 1. If p(4) > 0.025, retain H(4) and go to the next step. Otherwise reject all hypotheses and stop.
- Step 2. If p(3) > 0.025/2, retain H(3) and go to the next step. Otherwise reject all hypotheses and stop.
- Steps 3. If p(2) > 0.025/3, retain H(2) and go to the next step. Otherwise reject all remaining hypotheses and stop.
- Steps 4. If p(1) > 0.025/4, retain H(1) otherwise reject it.

The adjusted p-value is calculated as detailed below:

- Adjusted p(i) = p(4) for i = 4 other adjusted p(i) = minimum of [adjusted p(i+1), (5-i)*p(i)] for i = 3, 2, 1.

If any adjusted p-value exceeds 1, it is set to 1. Using this procedure, any adjusted p-value that is < 0.025 is statistically significant and supports a claim for the corresponding endpoint, while any adjusted p-value ≥ 0.025 is not statistically significant. Both adjusted and unadjusted p-values will be reported.

8.5.1 Sensitivity analyses of key secondary endpoints

The key secondary efficacy endpoints will be evaluated using the same sensitivity analyses for rescue intervention and missing data as those used for the primary efficacy endpoint (see Section

8.3.4). In addition, a sensitivity analysis for timing of baseline assessment will be performed to evaluate the impact of it on the secondary efficacy conclusions.

Sensitivity analysis for timing of baseline assessment

In this analysis, the baseline is defined as Day 0 assessments performed prior to randomization and initiation of stimulation.

8.5.2 Subgroup Analysis of Key Secondary Endpoints

The 4 key secondary endpoints will be summarized for the following subgroups:

- Number of prior biologic and targeted synthetic DMARDs (e.g., < 4 vs. ≥ 4)
- Prior use of JAKi (Yes vs. No)
- RA disease activity at informed consent (DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1)
- Moderate-to-severe RA at Day 0 (< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28)

8.6 Exploratory Secondary Endpoints

The exploratory secondary endpoints through Week 12 include:

- ACR50/70 response
- Component (TJC28, SJC28, Subject Pain, SGA, HAQ-DI, EGA, hsCRP) 20/50/70 response
- DAS28-CRP score change from baseline and LDA/remission
- CDAI score change from baseline, LDA/remission and MCID response
- Mean HAQ-DI score change from baseline
- RAMRIS bone erosion, osteitis, synovitis, and CARLOS score changes from baseline
- RAMRIS bone erosion progression (> 0.5) rate from baseline
- SF-36/PCS/MCS score change from baseline
- EQ-5D-5L score change from baseline and response
- Percent change in plasma biomarker concentrations (e.g., IL-1, SAA, MMP-3)

8.6.1 Definitions of Exploratory Secondary Endpoints

ACR50/70 response at Week 12

ACR50/70 response corresponds to 50% and 70% improvement at Week 12 from baseline on the day of informed consent, respectively, in TJC28 and SJC28 and 3 out of 5 ACR core measures and follows the same general and statistical analyses as for ACR20 (see Section **8.3.1**).

Component 20/50/70 response

20/50/70 response for each component (TJC28, SJC28, Subject Pain, SGA, HAQ-DI, EGA, hsCRP) corresponds to 20, 50 and 70% improvement from baseline to Week 12, respectively (see Section **8.2**), and follows the same general and statistical analyses as for ACR20 (see Section **8.3.1**).

DAS28-CRP score change and LDA/remission

The Disease Activity Score (DAS) is a derived measurement of 4 components with differential weighting:

- TJC28
- SJC28
- hsCRP (mg/L)
- SGA

A total score ranges from 0 to 10 and is computed as follows:

DAS28-CRP = 0.56 * sqrt(TJC28) + 0.28 * sqrt(SJC28) + 0.36 * ln(CRP+1) + 0.014 * SGA + 0.96

If one of the components is missing at an individual assessment point, the DAS28-CRP value for that assessment will be set to missing. An alternative imputation method for missing components may be applied as described in Section **8.1**.

The DAS28-CRP score corresponds to the current RA activity:

- 0 to < 2.6 Remission
- 2.6 to < 3.2 Low disease activity (LDA)
- 3.2 to ≤ 5.1 Moderate activity
- > 5.1 High activity

If one of the components is missing at a given assessment point, no imputations will be done, and the DAS28-CRP value for that assessment will be set to missing.

CDAI LDA/remission and MCID response at Week 12

The Clinical Disease Activity Index (CDAI) is a composite score consisting of the sum of:

- SJC28
- TJC28
- SGA/10
- EGA/10

The CDAI score is calculated as follows and ranges from 0 to 76 with higher values representing higher disease activity:

- CDAI = TJC28 + SJC28 + SGA + EGA

The CDAI score corresponds to the current RA activity:

- 0 to ≤ 2.8 Remission
- >2.8 to ≤ 10 Low disease activity (LDA)
- >10 to ≤ 22 Moderate activity
- > 22 High activity

The MCID varies depending on RA activity at baseline:

- -12 for high activity
- -6 for moderate activity
- 1 for low activity

If one of the components is missing at a given assessment point, no imputations will be done, and the CDAI value for that assessment will be set to missing. An imputation method for missing components may be applied as described in Section **5.8.1.**

HAQ-DI score change from baseline

Change from baseline on the day of inform consent to Week 12 in mean HAQ-DI score as determined by subjects (see Section **8.2.5**).

RAMRIS score and progression at Week 12

RAMRIS is the standardized system for RA MRI scoring of 4 different types of joint pathologies in the wrist and the hand. A total score for each pathology is generated by the summation of individual joint/bone scores as follows:

- *Synovitis*. 8 joints each scored on a scale from 0 = normal to 3 = severe, resulting in a total score from 0 to 24.
- *Bone erosion*. 25 bones each scored on a scale from 0 to 10, resulting in a total score from 0 to 250. An increase of > 0.5 from baseline to Week 12 will represent disease progression.
- *Osteitis*. 25 bones scored on a scale from 0 to 3, resulting in a total score from 0 to 75.
- *CARLOS (cartilage loss)*. 25 joints each scored on a scale from 0 to 4, resulting in a total score from 0 to 100.

Subjects will undergo MRI at Screening (baseline) and Week 12, and the MRI images will be scored by independent centralized blinded readers. Scores for each bone/joint will be calculated as the average of the score provided by each of the two readers. If a RAMRIS score from one of the readers is missing, then the RAMRIS score from the other reader will be used. If the score was

missing for both readers at any given time point, the average score is considered missing. An imputation method for missing components may be applied as described in Section **5.8.1**. A listing will be provided that presents change in total score from baseline by subject for each of the RAMRIS pathologies. The number of observations and the total score change mean, minimum, maximum and 95% confidence interval will be presented for the treatment and control groups in a table.

The smallest detectable change (SDC) will be calculated for each of the joint pathologies to assess whether a patient experienced a change beyond measurement error. The SDC is calculated as:

$\pm 1.96 \times SD_{\Delta(\text{CHANGE SCORES})} / (\sqrt{2} \times \sqrt{k})$

where CHANGE SCORE = change in RAMRIS total score between two timepoints, $SD_{\Delta(\text{CHANGESCORES})}$ represents the standard deviation of difference in change scores between the two readers, and k= the number of readers (Bruynesteyn et al., 2005).

In addition, subgroup analyses will be performed for subjects with and without baseline joint damage that is predictive of future progression (Gandjbakhch et al, 2014).

SF-36/PCS/MCS score change from baseline to Week 12

Health-related quality of life will be assessed using the subject-completed Medical Outcomes Study Short-Form 36 (SF-36), which is a generic health survey that contains 36 questions covering eight domains of health. The SF-36 yields an 8-scale profile of functional health and well-being scores as well as physical and mental component health summary scores. The version 2, 4-week recall questionnaire will be used. Recoding, calculations, and standardization will be done as recommended in the User's manual for the SF-36 (Mariush, 2011). Each of the 8 domain scores is the sum of some of the overall 36 item scores.

Domain scores will only be calculated if less than half of the item scores are missing. Missing item scores will be imputed as the mean of the other item scores within the same domain. If at least half of the item scores of a domain are missing, imputation will not be performed, and the domain will be set to missing. An imputation method for missing components may be applied as described in Section 5.8.1.

EQ-5D-5L response at Week 12

A standardized instrument for measuring general health status within the following 5 dimensions:

- Mobility
- Self-care
- Usual activities
- Pain/discomfort

- Anxiety/depression

Each dimension is scored on 5-point scale as:

- 1 = No problems
- 2 = Slight problems
- 3 = Moderate problems
- 4 = Severe problems
- 5 = Extreme problems/Unable

General health status is scored on a VAS (0 = poor to 100 = the best). An imputation method for missing components may be applied as described in Section **5.8.1.**

Reduction in the proportion of subjects with problems (moderate, severe or extreme) will represent improvement.

An EQ-5D summary index score can be derived by applying a formula that attached weights, or index values, to each of the levels in each dimension. The index is calculated by deducting the appropriate weights from the value for full health (i.e., 1). Value sets are country specific and can be obtained from the EuroQol website (EuroQol Research Foundation, 2023).

8.6.2 Analysis of Exploratory Secondary Endpoints

The following endpoints will be analyzed with the CMH test, as described in Section **5.1**:

- ACR50/70 response at Week 12
- DAS28-CRP LDA/remission at Week 12
- CDAI response at Week 12
- HAQ-DI response at Week 12
- EQ-5D-5L response at Week 12
- RAMRIS bone erosion progression (> 0.5) at Week 12

The MMRM will be used to analyze the following endpoints, as described in Section **5.1**:

- Mean CDAI score change from baseline to Week 12
- Mean HAQ-DI score change from baseline to Week 12
- Mean EQ-5D-5L score change from baseline to Week 12
- Mean SF-36/PCS/MCS score change from baseline to Week 12
- Mean RAMRIS bone erosion, osteitis, synovitis, and CARLOS score change from baseline to Week 12
- Percent change in plasma biomarkers (e.g., IL-6, SAA, MMP3)

8.7 Blinding Assessment

The effectiveness of blinding of subjects, joint evaluators and Co-PI Rheumatologists will be evaluated at Week 4 and Week 12 using a blinding questionnaire with the following questions:

- I strongly believe I am [or subject is] in the treatment group and receiving therapeutic stimulation
- I somewhat believe I am [or subject is] in the treatment group and receiving therapeutic stimulation
- I somewhat believe I am [or subject is] in the control group and receiving non-therapeutic stimulation
- I strongly believe I am [or subject is] in the control group and receiving non-therapeutic stimulation
- I don't know which group I am [or subject is] and which stimulation I am [or subject is] receiving

The statistical test will be Bang's blinding index (BI) and its associated 95% confidence interval (Bang 2010). The BI will be calculated for both the ITT and PTE populations.

9 SAFETY EVALUATION

9.1 AE and SAEs

The incidence of AEs and SAEs from informed consent date to Week 12 will be tabulated. Each AE will be evaluated by clinical investigators in terms of seriousness, severity (i.e., mild, moderate, severe) and strength of relationship (i.e., not related, unlikely related, probably related, definitely related, indeterminate) to the implant procedure, implant device, stimulation, Energizer, and explant procedure. Any AE that is determined by a participating investigator to be related (definitely related or probably related) to the implant procedure, implant device, stimulation, Energizer, or explant procedure will be categorized as device related. In unblinded analyses, if the subject was assigned to the control group, but the AE indicates relationship to stimulation, the AE relationship will be updated to "not related."

For all AE tables, a subject reporting the same adverse event more than once will be counted once when calculating the number and percentage of subjects with that particular event. If a subject reports the same AE more than once or has the same AE on multiple occasions, the maximum severity grade and relationship will be presented.

The frequencies and percentages of treatment-emergent adverse events will be presented by MedDRA system organ class (SOC) and preferred term (PT). Complete subject listings of all AE will be provided. For each AE the following will be specified: start and stop dates, severity grade, MedDRA SOC and PT, relationship (not related, unlikely related, probably related, definitely related, or indeterminate) to the implant procedure, implant device, stimulation, Energizer, and explant procedure, , as well as action taken, outcome of the adverse event, and seriousness.

9.2 Protocol Deviations

All protocol deviations will be tabulated with reasons for deviations, reviewed by sponsor using blinded data and reported in compliance with the study protocol, IRB requirements and sponsor's SOPs.

Protocol deviations will be categorized as major procedural if a study subject:

- Undergoes any study-related procedure before signing an IRB-approved informed consent form, or
- Receives study treatment not consistent with the treatment assignment, or
- Is no longer eligible but received study treatment.

Summary tables with the number and percentage of subjects with protocol deviations will be provided by treatment group and by type of deviation (**Appendix B**). A by-subject listing of all protocol deviations will be provided (**Appendix C**).

A sensitivity analysis for protocol deviations that could impact the primary endpoint will be performed to address potential bias from minor deviations. Protocol deviations will be reviewed by the Sponsor and those identified as possibly impacting the primary endpoint will be summarized in the CSR.

9.3 Device Deficiencies

All device deficiencies related to the identity, quality, durability, reliability, safety or performance of the study device, including device malfunctions, use errors, and inadequate labelling will be tabulated. Summary tables with the number and percentage of device deficiencies will be provided by type (**Appendix B**). A by-subject listing of all device malfunctions will be provided (**Appendix C**).

10 STATISTICAL CONSIDERATIONS RELATED TO COVID-19

The statistical considerations detailed in this section are consistent with the FDA's guidance on the conduct of clinical trials during the COVID-19 pandemic (Guidance for Industry on Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency; Issued June 2020) and recommendations for the statistical analysis of the primary and key secondary endpoints to help ensure that the COVID-19-related changes to the RESET-RA study conduct will provide interpretable findings with correct statistical quantification of uncertainty.

10.1 Impact of COVID-19 on Study Integrity

Unavoidable protocol modifications may be required due to COVID-19 illness and/or COVID-19 control measures to protect subject safety and the to address its impact on the ability to collect data. The context and/or reasons for post-baseline events as they relate to COVID-19, such as discontinuation of treatment, withdrawal from the trial, use of alternative or rescue treatments, missed endpoint assessments, and the use of alternative endpoint assessment methods will be

captured at the subject level. Information not specific to individual subjects, such as information on site closure (rheumatology or surgery) and its impact on disrupting administration of the investigational study device (i.e., implant procedure, device titration, device adjustments) will also be captured. This information at both the subject and site levels may be useful for incorporating into additional sensitivity analyses related to the impact of COVID-19.

10.2 COVID-19 Analysis Considerations

The impact of COVID-19 on the study integrity will be assessed and included into summaries of pooled data from Stage 1 and 2 over treatment groups, including information on missing data, protocol deviations, subject discontinuation or interruption of the investigational treatment, subject withdrawal, and changes in endpoint assessments (e.g., virtual visit).

To address adequately the impact of COVID-19 on evaluating the primary and key secondary endpoints, the following analysis strategies may be considered:

- If the study is stopped earlier than planned because of COVID-19, a smaller sample size or less follow-up time may result in loss of statistical power than was anticipated for the final analysis. A blinded power assessment will be conducted to estimate the power of the modified study. The assessment will use the actual event rates pooled over treatment group or the observed variability pooled over treatment group in the completed portion of the trial.
- Stopping the study earlier because of COVID-19 may impact the statistical inference (e.g., p-values, confidence intervals). Any modification to the study, including the original planned analyses, should not be based on data that reveal information on the treatment effect.
- If the study is stopped earlier because of COVID-19, the planned interim analysis may be appropriate for the statistical interference. Modifications can be considered to maintain control over Type 1 error. The actual results may be less statistically significant or have a wider confidence interval than the trial was designed for because of reduced information (e.g., fewer endpoint events).
- Extending the protocol-defined windows and using alternative remote methods for assessment of the primary and secondary efficacy endpoints may be warranted to address the impact of COVID-19. The data from these late or modified assessments can be leveraged based on scientifically based rationale and clinical judgement.
- Any differences in the assessment methods between treatment groups or among subjects with different baseline characteristics may be explored though sensitivity analyses stratified by the method and timing of the endpoint assessment. Additional sensitivity analyses will examine differences in baseline characteristics and post-baseline events (including endpoints and AEs) between the originally enrolled subjects and those with missing endpoint assessments or interrupted investigational treatment because of COVID-19.
- The available data at baseline and post-baseline, including COVID-19-related information will be leveraged using the prespecified methods for handling missing data in Section **5.8**. The analysis will take into consideration the actual event rates pooled over treatment groups or the observed variability pooled over treatment groups in the completed portion of the study.

11 REFERENCES

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12 APPENDICES

Appendix A: Schedule of Assessments

Assessment	Informed Consent & Screening (Baseline)	Enrollment & Implant Procedure (≤ 30d post-Informed Consent)	Post-Surgical Clearance (14-21d post-Implant Procedure)	Day 0 (Randomization & Initiation of Stimulation) (14-21d post-	Titration 1 (7 ± 2d2)	Titration 2 (14 ± 2d2)	Titration 3 (21 ± 2d2)	Week 4 (28 ± 3d2)	Week 8 (56 ± 5d2)	Week 12 (Primary Endpoint & One-way Crossover) (84 ± 7d2)
Informed consent	X*									
Vital signs	X*			X						X
Physical exam and medical history	X*									
Pregnancy test (childbearing female)	X*	X	X	X	X	X	X	X	X	X
RA disease activity assessments[1]	X*			X				X	X	X
RA prior and current medication	X*									
Energizer fit test	X*									
SF-36 & EQ-5D-5L questionnaires	X			X				X	X	X
Blood collection (RF, ACPA, eGFR)	X									
Blood collection (CBC, biomarkers)	X			X				X	X	X
Hand MRI	X									X
12-lead ECG	X									X
X-ray cervical spine	X									
Surgical clearance	X		X							
Implant procedure in operating room		X								
Randomization				X						
Subject training on the use of Energizer				X						
Device check & dose titration				X	X	X	X			X[3]
Device check & dose adjustment if needed								X	X	
Blinding assessment[4]								X		X
Treatment decision for long-term follow-up										X
Device deficiency reporting		X	X	X	X	X	X	X	X	X
Adverse event reporting	X	X	X	X	X	X	X	X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X

Abbreviations: ACPA, anti-citrullinated protein antibodies; CBC, complete blood count; d, day; EGA, evaluator's global assessment; eGFR: estimated glomerular filtration rate; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging; RA, rheumatoid arthritis; RF, rheumatoid factor; SGA, subject's global assessment; SJC, swollen joint count; TJC, tender joint count

* Screening assessments that must be conducted on the day of informed consent to determine subject's initial eligibility and baseline values for the primary and key secondary efficacy endpoints.

[1] RA disease activity assessments include: HAQ-DI, SGA, subject's pain assessment, TJC28, SJC28, EGA, and hsCRP. Subjects must have ≥ 4TJC28 and ≥ 4SJC28 at consent to be eligible.
[2] From Day 0 (randomization).
[3] Dose titration is not performed if subject and Co-PI Rheumatologist decide that subject should not receive active stimulation in open-label, long-term follow-up period.
[4] Blinding assessments are completed by the subject, Joint Evaluator and Co-PI Rheumatologist.

Appendix B: Table Mockups

Table 14.1.1.1
Subject Disposition
(All Subjects)

	Treatment	Control	All
Number of subjects:			
Consented	–	–	xxx
Screen failure	–	–	xxx
Enrolled	xxx	xxx	xxx
Implanted	xxx	xxx	xxx
Randomized	xxx	xxx	xxx
ITT population [1]	xxx	xxx	xxx
PTE population [2]	xxx	xxx	xxx
Safety population [3]	xxx	xxx	xxx
Withdrawn	xxx	xxx	xxx
Completed study through Week 12	xxx	xxx	xxx
Primary reason for withdrawal [4]:			
Subject decision to withdraw consent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Investigator decision or medical judgement	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Lost to follow-up	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Device malfunction	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Adverse event	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subject no longer eligible	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Death	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Study terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Sponsor or IRB decision	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Abbreviations: ITT, intent to treat; PTE, per-treatment-evaluable.
[1] ITT population comprises all enrolled and randomized subjects in Stage 1 and 2.
[2] PTE population comprises subjects from the ITT population who have received the assigned treatment, have no major procedural protocol deviations, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects in Stage 1 and 2.
[4] Percentage calculated based on ITT population.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Table 14.1.1.2
Demographic and Baseline Characteristics
(ITT Population)

	Treatment (N=xxx)	Control (N=xxx)	All (N=xxx)
N	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Age (years)			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.xx	xx.xx	xx.xx
Min-Max	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
Gender [1]			
Male	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Female	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Ethnicity [1]			
Hispanic or Latino	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Hispanic or Latino	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not disclosed	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Race [1][2]			
American Indian or Alaska Native	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Asian	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Black or African American	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Native Hawaiian or other Pacific Islander	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
White	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
RA duration (years)			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.xx	xx.xx	xx.xx
Min-Max	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
BMI (kg/m^2)			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)

	Treatment (N=xxx)	Control (N=xxx)	All (N=xxx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
RF [1]			
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ACPA [1]			
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Positive serology (RF and/or ACPA positive) [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
hsCRP (mg/L)			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
TJC28			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SJC28			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
CDAI score			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
DAS28-CRP score			

	Treatment (N=xxx)	Control (N=xxx)	All (N=xxx)
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
HAQ-DI score			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
EQ-5D-5L Index			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
EQ-VAS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SF-36 MCS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SF-36 PCS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
Number of prior b/ts DMARDs			

	Treatment (N=xxx)	Control (N=xxx)	All (N=xxx)
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
Number of prior b/ts DMARDs [1]			
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4			
5			
6			
7			
8			
9			
10+			
Prior b/ts DMARDs [1]			
Anti-IL-1 agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anti IL-6 agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anti-TNF agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
B-cell depleting agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
JAKi	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CTLA4-Ig	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Abbreviations: ACPA, anti-citrullinated protein antibodies; b/tsDMARD, biologic or targeted synthetic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; CTLA4-Ig, cytotoxic T-lymphocyte-associated antigen-4 immunoglobulin; DAS, Disease Activity Score; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high-sensitivity C-reactive protein; IL, interleukin; ITT, intent to treat; JAKi, Janus kinase inhibitor; RF, rheumatoid factor; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count; TNF, tumor necrosis factor.
[1] Percentage calculated based on ITT population.
[2] Race selected based on all that applied.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1
ACR20 Response
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 Response from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
ACR20 Response from Day 0*		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; ITT, intent to treat.
[1] Percentage calculated based on ITT population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
*Day 0 post-Implant Procedure and before randomization and initiation of assigned treatment

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.0
ACR20 Response
(PTE Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 Response from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
ACR20 Response from Day 0*		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; ITT, intent to treat.
[1] Percentage calculated based on ITT population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
*Day 0 post-Implant Procedure and before randomization and initiation of assigned treatment

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.1
Sensitivity Analysis of ACR20 Response: Rescue Treatment
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 Response from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
ACR20 Response from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

*Day 0 post-Implant Procedure and before randomization and initiation of assigned treatment

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.2
Sensitivity Analysis of ACR20 Response: Missing Data
(ITT Population)

Tipping Point Results	Treatment (N=xxx)	Control (N=xxx)	p-value
ACR20 Non-responder	xx	xx	0.xxx
ACR20 Responder	xx	xx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT population.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Note to biostats: If more than 5% of primary efficacy data are missing, the table above is to be presented in addition to the multiple imputation approach of Berglund and Heeringa (2014) described in SAP Section **8.3.4**.

Table 14.1.2.1.3
Sensitivity Analysis of ACR20 Response: Impact of COVID-19
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 Response from baseline on the day of informed consent		
No Covid-19 Diagnosis prior to Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Covid-19 Diagnosis prior to Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Interaction p-value [3]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects, and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
[3] Based on the Breslow Day test for homogeneity across subgroups.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.3.1
Descriptive Analysis of Diagnosis of COVID-19
(ITT Population)

	All (N=xxx)
Diagnosed with Covid-19 post-procedure	
N [1]	xx
Yes	xx (xx.x%)
Received medication/treatment for Covid-19	
N [1]	xx
Yes	xx (xx.x%)
Protocol Deviations associated with Covid-19 Diagnosis	
N [1]	xx
Yes	xx (xx.x%)
Adverse Events associated with Covid-19 Diagnosis	
N [1]	xx
Yes	xx (xx.x%)

Abbreviations: ITT, intent to treat.
[1] Percentage calculated based on ITT population.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.4
Subgroup Analysis of ACR20 Response: Age
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 Response from baseline on the day of informed consent		
Age < 65		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Age ≥ 65		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Interaction p-value [3]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
[3] Based on the Breslow Day test for homogeneity across subgroups.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.1.5
Subgroup Analysis of ACR20 Response: Gender
(ITT Population)

Repeat Table 14.1.2.1.5 for Gender [Male vs. Female]

Table 14.1.2.1.6
Subgroup Analysis of ACR20 Response: Race
(ITT Population)

Repeat Table 14.1.2.1.5 for Race [White vs. Non-White including Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander]

Table 14.1.2.1.7
Subgroup Analysis of ACR20 Response: RA Duration
(ITT Population)

Repeat Table 14.1.2.1.5 for RA Duration [< 5 years vs. ≥ 5 to < 10 years vs. ≥ 10 years]

Table 14.1.2.1.8
Subgroup Analysis of ACR20 Response: Prior b/tsDMARDs
(ITT Population)

Repeat Table 14.1.2.1.5 for Number of Prior b/tsDMARD [<4 vs. ≥ 4]

Add to abbreviations: *DMARD, disease-modifying antirheumatic drug;*

Table 14.1.2.1.9
Subgroup Analysis of ACR20 Response: Prior JAKi
(ITT Population)

Repeat Table 14.1.2.1.5 for Prior JAKi [Yes vs. No]

Add to abbreviations: *JAKi, Janus kinase inhibitor.*

Table 14.1.2.1.10
Subgroup Analysis of ACR20 Response: RA Disease Activity at Screening
(ITT Population)

Repeat Table 14.1.2.1.5 for RA Disease Activity at Screening [DAS28-CRP ≤ 5.1 vs DAS28-CRP > 5.1]

Add to abbreviations: *DAS, Disease Activity Score.*

Table 14.1.2.1.11
Subgroup Analysis of ACR20 Response: Moderate-to-severe RA at Day 0
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
Moderate-to-severe RA at Day 0		
< 4 TJC28 or < 4 SJC28		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
≥ 4 TJC28 and ≥ 4 SJC28		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Interaction p-value [3]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
[3] Based on the Breslow Day test for homogeneity across subgroups.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2
Key Secondary Endpoints Adjusted for Multiplicity
(ITT Population)

Endpoint	Unadjusted p-value	Adjusted p-value [1]
ACR20 response at Week 12 from baseline at Day 0	x.xxxx	x.xxxx
DAS28-CRP moderate/good EULAR response at Week 12 from baseline on the day of informed consent	x.xxxx	x.xxxx
DAS28-CRP response (MCID ≥ -1.2) at Week 12 from baseline on the day of informed consent	x.xxxx	x.xxxx
HAQ-DI response (MCID ≥ -0.22) at Week 12 from baseline on the day of informed consent	x.xxxx	x.xxxx

Abbreviations: CRP, C-reactive protein; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent to treat; MCID, minimal clinically important difference.
[1] Adjusted for multiplicity using Hochberg's Step-Up Method

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2.1
Key Secondary Endpoints
(PTE Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
DAS28-CRP moderate/good EULAR response at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
DAS28-CRP response (MCID ≥ -1.2) at Week 12		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
HAQ-DI response (MCID ≥ -0.22) at Week 12		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
Mean HAQ-DI score change at Week 12		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; CRP, C-reactive protein; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent to treat; MCID, minimal clinically important difference.

Variable	Treatment (N=xxx)	Control (N=xxx)

[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2.2
Sensitivity Analysis of Key Secondary Endpoints: Timing of Baseline
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
DAS28-CRP moderate/good EULAR response at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
DAS28-CRP response (MCID ≥ -1.2) at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
HAQ-DI response (MCID ≥ -0.22) at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
Mean HAQ-DI score change at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Variable	Treatment (N=xxx)	Control (N=xxx)

Abbreviations: ACR, American College of Rheumatology; CRP, C-reactive protein; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent to treat; MCID, minimal clinically important difference.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2.3
Sensitivity Analysis of Key Secondary Endpoints: Rescue Treatments
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 response at Week 12 from Day 0		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
DAS28-CRP moderate/good EULAR response at Week 12 from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
DAS28-CRP response (MCID ≥ -1.2) at Week 12 from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	
HAQ-DI response (MCID ≥ -0.22) at Week 12 from baseline on the day of informed consent		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	

Variable	Treatment (N=xxx)	Control (N=xxx)

Abbreviations: ACR, American College of Rheumatology; CRP, C-reactive protein; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent to treat; MCID, minimal clinically important difference.

[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2.4
Sensitivity Analysis of Key Secondary Endpoints: Missing Values
(ITT Population)

Insert 2 x 2 table with tipping point results

Note to biostats: If more than 5% of primary efficacy data are missing, the table above is to be presented in addition to the multiple imputation approach of Berglund and Heeringa (2014) described in SAP Section 8.3.4.

Table 14.1.2.2.5
Subgroup Analysis of Key Secondary Endpoints: Prior b/tsDMARDs
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR20 response from Day 0		
< 4 Prior b/tsDMARD		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
≥ 4 Prior b/tsDMARD		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Interaction p-value [3]	0.xxx	
Repeat for:		
DAS28-CRP moderate/good EULAR response at Week 12 from baseline		
DAS28-CRP response (MCID ≥ -1.2) at Week 12 from baseline		
HAQ-DI response (MCID ≥ -0.22) at Week 12 from baseline		

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Variable	Treatment (N=xxx)	Control (N=xxx)

[3] Based on the Breslow Day test for homogeneity across subgroups.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.2.6
Subgroup Analysis of Key Secondary Endpoints: Prior JAKi
(ITT Population)

Repeat Table 14.1.2.2.5 for Prior JAKi [Yes vs. No]

Table 14.1.2.2.7
Subgroup Analysis of Key Secondary Endpoints: RA Disease Activity at Screening
(ITT Population)

Repeat Table 14.1.2.2.5 for RA Disease Activity at Screening [DAS28-CRP ≤ 5.1 vs DAS28-CRP > 5.1]

Table 14.1.2.2.8
Subgroup Analysis of Key Secondary Endpoints: Moderate-to-severe RA at Day 0
(ITT Population)

Repeat Table 14.1.2.2.5 for Moderate-to-severe RA at Day 0 [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Table 14.1.2.3
ACR50/70
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
ACR50 Response		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
ACR70 Response		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: ACR, American College of Rheumatology; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test stratified by inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.4
TJC28
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
TJC28 Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
TJC28 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
TJC28 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
TJC28 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: TJC, tender joint count for 28 different joints; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 For Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.5
SJC28
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
SJC28 Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)

Variable	Treatment (N=xxx)	Control (N=xxx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]f	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SJC28 20% Response [1]		
Week 12		
N [1]	xx	xx

Variable	Treatment (N=xxx)	Control (N=xxx)
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SJC28 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SJC28 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: SJC, swollen joint count for 28 different joints; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.6
Subject's Assessment of Pain
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
Subject's Pain Assessment (NRS)		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Subject's Pain 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Subject's Pain 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Subject's Pain 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: NRS, Numerical Rating Scale; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.7
SGA
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
SGA Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SGA 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SGA 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
SGA 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: SGA, subject's global assessment; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.8
EGA
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
EGA Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
EGA 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
EGA 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
EGA 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: EGA, evaluator's global assessment; ITT, intent to treat.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.9
hsCRP
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
hsCRP (mg/L)		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
hsCRP 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
hsCRP 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
hsCRP 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: hsCRP, high sensitivity C-reactive protein; ITT, intent to treat..
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.10
HAQ-DI
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
HAQ-DI Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI 20% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI 50% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI 70% Response [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI Mild Difficulties to Moderate Disability (score from 0 to < 1) [1]		
Screening (baseline)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI Moderate Disability (score from 1 to < 2) [1]		
Screening (baseline)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)

Variable	Treatment (N=xxx)	Control (N=xxx)
Difference [2]	xx.x%	
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI Subjects with Severe to Very Severe Disability (score from 2 to 3) [1]		
Screening (baseline)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
HAQ-DI Response (MCID ≥ 0.22) [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent to treat; MCID, Minimal clinically important difference.

[1] Percentage calculated based on ITT Population

[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Variable	Treatment (N=xxx)	Control (N=xxx)

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.11
DAS28-CRP
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
DAS28-CRP Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
DAS28-CRP MCID Response (score reduction from Baseline by 1.2) [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
DAS28-CRP Low Disease Activity (score 2.6 to < 3.2) [1]		
Week 12		
N [1]		
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
DAS28-CRP Remission (score 0 to < 2.6) [1]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
DAS28-CRP EULAR Good Response [1][3]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
DAS28-CRP EULAR Moderate Response [1][4]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: CRP, C-reactive protein; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; ITT, intent to treat.
[1] Percentage calculated based on ITT Population

Variable	Treatment (N=xxx)	Control (N=xxx)

[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.
[3] EULAR good treatment response if DAS28-CRP score reduced from baseline to a given timepoint by > 1.2 and is ≤ 3.2 at a given timepoint
[4] EULAR moderate treatment response if DAS28-CRP score reduced from baseline to a given timepoint by > 0.6 to ≤ 1.2, and is ≤ 5.1 at a given timepoint; or DAS28-CRP score reduced from baseline to a given timepoint by > 1.2, and is > 3.2 at a given timepoint

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.12
CDAI
(ITT Population)

	Treatment (N=xxx)	Control (N=xxx)
CDAI Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
CDAI Low Disease Activity (Score >2.8 to ≤ 10) [1]		
Screning (baseline)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	

	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
CDAI Remission (Score 0 to ≤ 2.8) [1]		
Screening (baseline)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
CDAI Response (MCID) [1][3]		
Week 12		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: CDAI, Clinical Disease Activity Index; ITT, intent to treat; MCID, Minimal clinically important difference.
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease

	Treatment (N=xxx)	Control (N=xxx)

severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

[3] MCID is -12 if starting in high disease (> 22), -6 if starting in moderate disease (10-22); and 1 if starting in low disease (< 10).CDAI ranges from 0 to 76 with higher values representing higher disease activity.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.13
RAMRIS
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
RAMRIS Bone Erosion Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline (SDC: x.xx)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Progression rate from baseline (> 0.5)		
N [1]	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)
Difference [2]	xx.x%	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
RAMRIS Osteitis Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)

Variable	Treatment (N=xxx)	Control (N=xxx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline (SDC: x.xx)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
RAMRIS Synovitis Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline (SDC: x.xx)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	

Variable	Treatment (N=xxx)	Control (N=xxx)
p-value for difference [2]	0.xxx	
RAMRIS CARLOS Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline (SDC: x.xx)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: CARLOS, cartilage loss score; ITT, intent to treat; RAMRIS, Rheumatoid Arthritis MRI Scoring System; SDC, Smallest Detectable Change
[1] Percentage calculated based on ITT Population.
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Difference in proportions and one-sided p-value based on the Cochran-Mantel-Haenszel test. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.14
EQ-5D-5L
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
EQ-5D-5L Index Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx

Variable	Treatment (N=xxx)	Control (N=xxx)
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
EQ-5D-5L Mobility Dimension [1]		

Variable	Treatment (N=xxx)	Control (N=xxx)
Screening (baseline)		
Level 1 (No problem)	xx (xx.x%)	xx (xx.x%)
Level 2 (Slight problems)	xx (xx.x%)	xx (xx.x%)
Level 3 (Moderate problems)	xx (xx.x%)	xx (xx.x%)
Level 4 (Severe problems)	xx (xx.x%)	xx (xx.x%)
Level 5 (Extreme problems)	xx (xx.x%)	xx (xx.x%)
Repeat each level for: Day 0, Week 4, Week 8, and Week 12		
Repeat for other dimensions:		
EQ-5D-5L Self-care		
EQ-5D-5L Usual activities		
EQ-5D-5L Pain/discomfort		
EQ-5D-5L Anxiety/depression		
EQ VAS		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Variable	Treatment (N=xxx)	Control (N=xxx)
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Difference [2]	xx (xx.x%)	
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	

Abbreviations: EQ-5D-5L, EuroQol 5 domains 5 levels; ITT, intent to treat.
[1] Percentage calculated based on ITT Population
[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.15
SF-36
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
SF-36 MCS Score		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	Treatment (N=xxx)	Control (N=xxx)
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI for difference [2]	(xx.x, xx.x)	
p-value for difference [2]	0.xxx	
Repeat for: SF-36 PCS Score		

Abbreviations: ITT, intent to treat; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Short Form Survey with 36 items.
[1] Percentage calculated based on ITT Population

Variable	Treatment (N=xxx)	Control (N=xxx)

[2] Difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.16
Subject's Blinding Assessment
(ITT Population)

Assignment	Subject believes he/she was in					BI
	Treatment Strongly Believe	Treatment Somewhat Believe	Control Somewhat Believe	Control Strongly Believe	Don't Know	(95% CI)
Week 4						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Week 12						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)

Abbreviations: BI, Bang's blinding index; ITT, intent to treat.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.16.1
Subject's Blinding Assessment
(PTE Population)

Repeat Table 14.2.16 for PTE population

Table 14.1.2.17
Joint Evaluator's Blinding Assessment
(ITT Population)

Assignment	Evaluator believes subject is in					BI
	Treatment Strongly Believe	Treatment Somewhat Believe	Control Somewhat Believe	Control Strongly Believe	Don't Know	(95% CI)
Week 4						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Week 12						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)

Abbreviations: BI, Bang's blinding index; ITT, intent to treat.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.17.1
Evaluator's Blinding Assessment
(PTE Population)

Repeat Table 14.2.17 for PTE population

Table 14.1.2.18
Co-PI Rheumatologist's Blinding Assessment
(ITT Population)

Assignment	Co-PI Rheumatologist believes subject is in					BI
	Treatment Strongly Believe	Treatment Somewhat Believe	Control Somewhat Believe	Control Strongly Believe	Don't Know	(95% CI)
Week 4						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Week 12						
Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)
Control	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xx (0.xx, 0.xx)

Abbreviations: BI, Bang's blinding index; ITT, intent to treat.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.18.1
Co-PI Rheumatologist's Blinding Assessment
(PTE Population)

Repeat Table 14.2.18 for PTE population

Table 14.1.2.19
Inflammatory Biomarkers
(ITT Population)

Variable	Treatment (N=xxx)	Control (N=xxx)
IL-6 (pg/mL)		
Screening (baseline)		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Day 0		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 4		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 8		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 12		
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline		

Variable	Treatment (N=xxx)	Control (N=xxx)
N [1]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Percent change	xx.x%	xx.x%
Relative difference [2]	xx.x%	
95% CI for difference [2]	(xx.x%, xx.x%)	
p-value for difference [2]	0.xxx	

Repeat for:
SAA (µg/mL)
MMP-3 (pg/mL)

Abbreviations: IL, interleukin; ITT, intent to treat; MMP, matrix metalloproteinase; SAA, serum amyloid A.
[1] Percentage calculated based on ITT Population.
[2] Relative difference in mean score change from baseline and one-sided p-value based on the Mixed-effect Model Repeated Measure model with PROC MIXED. Stratification factors are inadequate response or loss of response to JAKi and RA disease severity at Day 0 for Stage 1 subjects and RA disease severity at Day 0 and inadequate response or loss of response to ≥ 4 biological DMARDs with ≥ 2 mechanisms of action for Stage 2 subjects.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.20
RA Rescue Treatments and Follow-up Interventions
(ITT Population)

	Treatment (N=xxx)	Control (N=xxx)
Received any post-procedure RA rescue treatment		
Yes [1]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [2]	xxx (xx.x%)	xxx (xx.x%)
Post-Surgical Clearance	xxx (xx.x%)	xxx (xx.x%)
Day 0	xxx (xx.x%)	xxx (xx.x%)
Titration 1	xxx (xx.x%)	xxx (xx.x%)
Titration 2	xxx (xx.x%)	xxx (xx.x%)
Titration 3	xxx (xx.x%)	xxx (xx.x%)
Week 4	xxx (xx.x%)	xxx (xx.x%)
Week 8	xxx (xx.x%)	xxx (xx.x%)
Week 12	xxx (xx.x%)	xxx (xx.x%)
Received csDMARD for RA (other than 1 at stable dose from Informed Consent to Week 12, as required per protocol) [1]		
Yes [1]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [2]	xxx (xx.x%)	xxx (xx.x%)
Post-Surgical Clearance	xxx (xx.x%)	xxx (xx.x%)
Day 0	xxx (xx.x%)	xxx (xx.x%)
Titration 1	xxx (xx.x%)	xxx (xx.x%)
Titration 2	xxx (xx.x%)	xxx (xx.x%)
Titration 3	xxx (xx.x%)	xxx (xx.x%)
Week 4	xxx (xx.x%)	xxx (xx.x%)
Week 8	xxx (xx.x%)	xxx (xx.x%)
Week 12	xxx (xx.x%)	xxx (xx.x%)
Received b/tsDMARDs for RA [1]		
Yes [1]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [2]	xxx (xx.x%)	xxx (xx.x%)
Post-Surgical Clearance	xxx (xx.x%)	xxx (xx.x%)
Day 0	xxx (xx.x%)	xxx (xx.x%)
Titration 1	xxx (xx.x%)	xxx (xx.x%)
Titration 2	xxx (xx.x%)	xxx (xx.x%)

	Treatment (N=xxx)	Control (N=xxx)
Titration 3	xxx (xx.x%)	xxx (xx.x%)
Week 4	xxx (xx.x%)	xxx (xx.x%)
Week 8	xxx (xx.x%)	xxx (xx.x%)
Week 12	xxx (xx.x%)	xxx (xx.x%)
Received corticosteroids (equivalent >10mg/day average dose prednisone) for RA [1]		
Yes [1]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [2]	xxx (xx.x%)	xxx (xx.x%)
Post-Surgical Clearance	xxx (xx.x%)	xxx (xx.x%)
Baseline	xxx (xx.x%)	xxx (xx.x%)
Titration 1	xxx (xx.x%)	xxx (xx.x%)
Titration 2	xxx (xx.x%)	xxx (xx.x%)
Titration 3	xxx (xx.x%)	xxx (xx.x%)
Week 4	xxx (xx.x%)	xxx (xx.x%)
Week 8	xxx (xx.x%)	xxx (xx.x%)
Week 12	xxx (xx.x%)	xxx (xx.x%)
Repeat for other RA rescue treatments as reported in CRFs		

Abbreviations: b/tsDMARD, biologic or targeted synthetic disease-modifying anti-rheumatic drug.
[1] Percentage calculated based on ITT Population.
[2] Percent is calculated based on the start date noted on the Concomitant Medication log.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.2.22
Implant Performance
(ITT Population)

Variable	Treatment	Control	All
Status of Study Implant at Study Exit [1]	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with active implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with deactivated/decommissioned implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with explanted implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unknown	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

[1] Percentage calculated based on ITT Population.
Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Table 14.1.3.1
Adverse Events
(Safety Population)

Variable	Treatment (N=xxx) Events n (%)	Control (N=xxx) Events n (%)	All (N=xxx) Events n (%)
Any AE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Not Related	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Related [1]			
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Indeterminate			
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE resulting in discontinuation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE by maximum severity			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure AE by maximum severity			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Variable	Treatment (N=xxx) Events n (%)	Control (N=xxx) Events n (%)	All (N=xxx) Events n (%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device AE by maximum severity			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation AE by maximum severity			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure AE by maximum severity [1]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
SAE [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Energizer SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; RA, rheumatoid arthritis; SAE, serious adverse event.

Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE.

[1] AEs judged to be "Definitely related" or "Probably related" are reported as "Related".

Reference: Listing 16.x.x.x

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.3.2
Adverse Events by SOC and Maximum Severity: All Events
Safety Population

SOC Preferred Term	Treatment (N=xxx)				Control (N=xxx)				All (N=xxx)			
	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)
Prior to Implant Procedure												
Any AE [1]	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 (xx%)
SOC 1 [1]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xxxx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)	xx x (xx%)
SOC 2 [1]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)

SOC Preferred Term	Treatment (N=xxx) Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Control (N=xxx) Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	All (N=xxx) Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)
Continue to report all reported events												
<u>At and Post-Implant Procedure</u>												
Any AE [1]	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 (xx%)
SOC 1 [1]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
SOC 2 [1]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
Continue to report all reported events												

SOC Preferred Term	Treatment (N=xxx)				Control (N=xxx)				All (N=xxx)			
	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)

Abbreviations: AE, adverse event; SOC, system organ class.
Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE.
[1] Percentage calculated based on ITT Population.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.3.3
Implant Procedure-Related Adverse Events by SOC and Maximum Severity: All Events
(Safety Population)

SOC Preferred Term	Treatment (N=xxx)				Control (N=xxx)				All (N=xxx)			
	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)
Subjects with any AE [1,2]	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 (xx%)
System Organ Class 1 [1,2]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
System Organ Class 2 [1,2]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
Continue to report all reported events												

Abbreviations: AE, adverse event; SOC, system organ class.
Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE.
[1] Percentage calculated based on ITT Population.
[2] AEs judged to be "Definitely Related" or "Probably Related" " to Implant Procedure are reported.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.3.4
Implant Device-Related Adverse Events by SOC and Maximum Severity: All Events
(Safety Population)

Repeat Table 14.1.3.4 for implant device-related adverse events

Table 14.1.3.5
Stimulation-Related Adverse Events by SOC and Maximum Severity: All Events
(Safety Population)

Repeat Table 14.1.3.4 for stimulation-related adverse events

Table 14.1.3.6
Explant Procedure-Related Adverse Events by SOC and Maximum Severity: All Events
(Safety Population)

Repeat Table 14.1.3.4 for explant procedure-related adverse events

Table 14.1.3.7
Energizer-Related Adverse Events by SOC and Maximum Severity: All Events
(Safety Population)

Repeat Table 14.1.3.4 for Energizer-related adverse events

Table 14.1.3.8
Device Deficiency
(Safety Population)

Variable	Treatment (N=xxx) Events n (%)	Control (N=xxx) Events n (%)	All (N=xxx) Events n (%)
Any study device deficiency [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Relationship of study device deficiency [1]			
MicroRegulator (Implant)	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
POD	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Energizer	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Prescription Pad	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
IFU/Labeling	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Study device deficiency associated with AE [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Study device deficiency associated with SAE [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; POD, Positioning Orientation Device; SAE, serious adverse event.
Note: Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subject experiencing several episodes of the same type of study device deficiency is counted once.
[1] Percentage calculated based on safety ITT population.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.1.3.9
Protocol Deviations
(ITT Population)

Variable	Treatment (N=xxx) Events n (%)	Control (N=xxx) Events n (%)	All (N=xxx) Events n (%)
Any protocol deviations [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Any major procedural protocol deviations	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Consent not obtained prior to initiating any study-related procedures	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Received study treatment not consistent with the treatment assignment	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Subject not eligible received treatment procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Minor protocol deviations [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Improper documentation of consent	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment not done	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment completed out of window	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE not reported within required schedule	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Received medication not allowed per protocol	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Subject or study staff unblinded	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Other, specify	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations due to COVID-19 [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations associated with AE [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations associated with SAE [1]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; SAE, serious adverse event.
Note: Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once.
[1] Percentage calculated based on safety ITT population.
Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Appendix C: Listing Mockups

Listing 16.1.1
Eligibility and Treatment Assignment

Subject ID	Enrolled	Randomized	Randomization Number	Randomization Date	Treatment Assignment
xx-xxxx	Yes	Yes	xx-xx	DD-MMM-YYYY	Treatment
xx-xxxx	Yes	Yes	xx-xx	DD-MMM-YYYY	Control

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.1.1
Subject Disposition

Treatment Group	Subject ID	Consent Date	Implant Procedure Date	Randomization Date	Subject Status	Date of Exit	Reason for Withdrawal	Implant Status at Study Exit
	xx-xxxx	DD-MMM-YYYY	DD-MMM-YYYY	DD-MMM-YYYY				

Programming note: This listing will include all consented subjects including screen failures, all other listings should only include all enrolled subjects.

Subject Status: Consented, Screen Failure, Enrolled, Implanted, Randomized, Withdrawn, Completed Study

Reason for withdrawal: Subject decision to withdraw consent, Investigator decision or medical judgement, Lost to follow-up, Device malfunction, Adverse event, Subject no longer eligible, Death, Study terminated, Sponsor or IRB decision, Other

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.1.2
Eligibility Not Met

Subject ID	Date of Screening Visit DD-MMM-YYYY	Inclusion		Exclusion	
		Met All?	Criteria Not Met	Met Any?	Criteria Met
xx-xxxx	DD-MMM-YYYY (-x)	Yes		Yes	xx-xxxxxxxxxxxxxxxxxxxxxxxxxxxx
xx-xxxx	DD-MMM-YYYY (-x)	No	xx -xxxxxxxxxxxxxxxxxx	No	
xx-xxxx	DD-MMM-YYYY (-x)	Yes		No	

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.2
Protocol Deviations

Treatment Group	Subject ID	Deviation ID	Visit	Deviation Date	Classification	Category	Reason	Associated with AE?	Associated with SAE?	Reported to IRB?	Description
Treatment	xx-xxxx										
Control	xx-xxxx										

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.3
Analysis Populations

Treatment Group	Subject ID	Population		Reason for Exclusion from PTE
		ITT [1]	PTE [2]	
Treatment	xx-xxxx	Yes	Yes	
Treatment	xx-xxxx	No	Yes	
Control	xx-xxxx	No	Yes	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Abbreviations: ITT, intent to treat; PTE, per-treatment-evaluable; RA, rheumatoid arthritis.
[1] ITT population comprises all enrolled and randomized subjects in Stage 1 and 2
[2] PTE population comprises subjects from ITT population who have received the assigned treatment, have no major procedural protocol deviations, and for whom follow-up data are available

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.4
Demographics and Baseline Characteristics
(Part 1)

Treatment Group	Subject ID	Age (year)	Gender	Ethnicity	Race	RA Duration (year)	BMI (kg/m^2)	RF	ACPA	hsCRP (mg/L)	TJC28	SJC28
Treatment	xx-xxxx	xx	F	Non-Hispanic	White			Negative	Positive			
Control		xx	M	Hispanic	White			Positive	Negative			

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.4
Demographics and Baseline Characteristics
(Part 2)

Treatment Group	Subject ID	CDAI Score	DAS28-CRP Score	HAQ-DI Score	Number of Prior b/tsDMARDs	Prior b/tsDMARDs	Prior Jaki (Y/N)	Ongoing Medical Condition
Treatment	xx-xxxx							
Control								

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.5.1
Subjects Receiving Rescue Treatment Prior to Week 12 (ITT Population)

Subject ID	CDAI at baseline	CDAI prior to start of rescue	Type of rescue	Start date / Stop date	Rescue type ongoing in OL/LTFU (Y/N)	Rescue start relative to Day 0 (days)
xx-xxxx	Baseline: xx.x	Day 0: xx.x				

Listing 16.1.2.5.1
Prior and Concomitant Medication

Treatment Group	Subject ID	ATC level Preferred Term/ Medication	Start Date	Start Study Day	Stop Date	Stop Study Day	Primary Indication	Dosage (Unit)	Route	Frequency
	xx-xxxx									
	xx-xxxx									

Programming Note:

1. If Ongoing is checked "Yes" list "Ongoing" under stop date column
2. Concatenate dose and unit for listing, if other unit exists then list it for units
3. Route, if Other Route is not blank, list it under "Route" column
4. Frequency, if Other Frequency is not blank, list it under 'Frequency" Column

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.5.2
Implant and Explant Procedure

Treatment Group	Subject ID	Procedure Date	MicroRegulator Serial#	Procedure Start Time	Procedure Stop Time	Procedure type (Implant/Explant)	Post-Op Clearance Date
	xx-xxxx						
	xx-xxxx						

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.5.3
Stimulation Prescription
(Part 1)

Treatment Group	Subject ID	Visit	Strength (uA)	Duration	Frequency	Schedule	Dose Changed at this Visit?	Dose Change Reason
	xx-xxxx							
	xx-xxxx							

Listing 16.1.2.5.3
Stimulation Prescription
(Part 2)

Treatment Group	Subject ID	Energizer App Firmware	Energizer Bluetooth Firmware	Implant App Firmware	Implant Impedance	MicroRegulator Suspended?/ Reason
	xx-xxxx					
	xx-xxxx					

Listing 16.1.2.6.1
RA Disease Activity Assessments

Treatment Group	Subject ID	Visit	SJC28	TJC28	HAQ-DI Score	Subject's Pain	Subject's Global Assessment	Evaluator's Global Assessment	hsCRP (mg/mL)
Treatment	xx-xxxx	Screening Day 0 Week 4 Week 8 Week 12	xx	xx	xxx	xxx	xx	xxx	xx
Control	xx-xxxx								

SOURCE: xxxxx SAS 9.4 {program location}

Listing 16.1.2.6.2
ACR20 Response from Baseline on the Day of Informed Consent

Treatment Group	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI Score	Subject's Pain	Subject's Global Assessment	Evaluator's Global Assessment	hsCRP (mg/mL)
Treatment	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	N	N	N	N	N	N	N	N
		Week 8	Y	N	N	N	N	N	N	N
		Week 12	Y	Y	Y	N	Y	Y	**N**	**Y**
Control	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	Y	N	N	N	N	N	N	N
		Week 8	N	N	N	N	N	N	N	N
		Week 12								

Note: Response defined by at least 20% reduction from baseline on the day of informed consent in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.2.1
ACR20 Response from Day 0

Treatment Group	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI Score	Subject's Pain	Subject's Global Assessment	Evaluator's Global Assessment	hsCRP (mg/mL)
Treatment	xx-xxxx	Week 4	N	N	N	N	N	N	N	N
		Week 8	Y	N	N	N	N	N	N	N
		Week 12	Y	Y	Y	N	Y	Y	**N**	**Y**
Control	xx-xxxx	Week 4	N	N	N	N	N	N	N	N
		Week 8	Y	N	N	N	N	N	N	N
		Week 12	Y	Y	Y	N	Y	Y	**N**	**Y**

Note: Response defined by at least 20% reduction from Day 0 in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.2
ACR50 Response

Treatment Group	Subject ID	Visit	ACR50 Response	SJC28	TJC28	HAQ-DI Score	Subject's Pain	Subject's Global Assessment	Evaluator's Global Assessment	hsCRP (mg/mL)
Treatment	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	Y	N	N	N	N	N	N	N
		Week 8	Y	Y	Y	N	Y	Y	**N**	**Y**
		Week 12								
Control	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	Y	N	N	N	N	N	N	N
		Week 8	N	N	N	N	N	N	N	N
		Week 12								

Note: Response defined by at least 50% reduction from baseline on the day of informed consent in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.2
ACR70 Response

Treatment Group	Subject ID	Visit	ACR70 Response	SJC28	TJC28	HAQ-DI Score	Subject's Pain	Subject's Global Assessment	Evaluator's Global Assessment	hsCRP (mg/mL)
Treatment	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	Y	N	N	N	N	N	N	N
		Week 8	Y	Y	Y	N	Y	Y	**N**	**Y**
		Week 12								
Control	xx-xxxx	Day 0	N	N	N	N	N	N	N	N
		Week 4	Y	N	N	N	N	N	N	N
		Week 8	N	N	N	N	N	N	N	N
		Week 12								

Note: Response defined by at least 70% reduction from baseline on the day of informed consent in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.5
CDAI

Treatment Group	Subject ID	Visit	CDAI Score	CDAI LDA (>2.8 to ≤ 10)	CDAI Remission (0 to ≤ 2.8)	CDAI MCID Response
Treatment	xx-xxxx	Screening	xx.x	--	--	--
		Day 0		--	--	--
		Week 4		No	No	No
		Week 8		Yes	No	Yes
		Week 12		Yes	Yes	Yes

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.6
DAS28-CRP

Treatment Group	Subject ID	Visit	DAS28-CRP Score	DAS28-CRP LDA (0.6 to < 3.2)	DAS28-CRP Remission (0 to < 2.6)	DAS28-CRP MCID Response (-1.2)	DAS28-CRP Good/Moderate EULAR Response
Treatment	xx-xxxx	Screening	xx	–	--	--	--
		Day 0	xx	–	--	--	--
		Week 4	xx	No	No	No	
		Week 8	xx	Yes	No	Yes	Moderate
		Week 12	xx	Yes	Yes	Yes	Good

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.7
HAQ-DI

Treatment Group	Subject ID	Visit	HAQ-DI Score	HAQ-DI Response (MCID -0.22)
Treatment	xx-xxxx	Screening	xx	--
		Day 0	xx	No
		Week 4	xx	No
		Week 8	xx	Yes
		Week 12	xx	Yes

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.8
RAMRIS

Treatment Group	Subject ID	Visit	Synovitis score	Osteitis score	Bone erosion score	Progression? (bone erosion increase > 0.5)	CARLOS
Treatment	xx-xxxx	Screening Week 12 Change from baseline				-- No	

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.9
EQ-5D-5L

Treatment Group	Subject ID	Visit	Mobility	Self-Care	Usual Activities	Pain/Discomfort	Anxiety/Depression	EQ-VAS	Index value
Treatment	xx-xxxx	Screening Day 0 Week 4 Week 8 Week 12	x	x	x	x	x	xxx	xx

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.10
SF-36

Treatment Group	Subject ID	Visit	PCS score	MCS score
Treatment	xx-xxxx	Screening Day 0 Week 4 Week 8 Week 12		

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.11
Inflammatory Biomarkers

Treatment Group	Subject ID	Visit	IL-6 (pg/mL)	IL-6 % Change	SAA (µg/mL)	SAA % Change	MMP-3 (pg/mL)	MMP-3 % Change
Treatment	xx-xxxx	Screening		--		--		--
		Day 0		--		--		--
		Week 4						
		Week 8						
		Week 12						

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.12
Subject's Blinding Assessment

Treatment Group	Subject ID	Visit Date (Study Day)	Week 4	Why?	Week 12	Why?
xxx	xx-xxxx					

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.13
Joint Evaluator's Blinding Assessment

Treatment Group	Subject ID	Visit Date (Study Day)	Week 4	Why?	Week 12	Why?
xxx	xx-xxxx					

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.6.14
Co-PI Rheumatologist's Blinding Assessment

Treatment Group	Subject ID	Visit Date (Study Day)	Week 4	Why?	Week 12	Why?
xxx	xx-xxxx					

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.7
Adverse Events

Treatment Group	Subject ID	System Organ Class/ Preferred Term/ Adverse Event Verbatim	Onset Date (Day)	Resolution Date (Day)	Severity	SAE?	Relationship	Treatment/ outcome
Treatment	xx-xxxx	xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/	DD-MMM-YYYY (xx)	DD-MMM-YYYY (xx)				xxxxxx/ xxxxxx
Control	xx-xxxx	None						

Note: If a Subject has no AEs then "None" will be displayed. Adverse Events are coded in MedDRA.

Programming Note: If Ongoing is checked then list “Continuing” in the place for “Resolution Date (Day)”.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.1.2.8
Device Deficiencies

Treatment Group	Subject ID	Deficiency ID	Deficiency Date	Deficiency Related To	Associated with AE?	Associated with SAE?	Description
Treatment	xx-xxxx						
Control	xx-xxxx						

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

STATISTICAL ANALYSIS PLAN

For Long-Term Safety and Exploratory Analyses

1 TITLE PAGE

Study Title	Vagus Nerve Stimulation Using the SetPoint System for Moderate-to-Severe Rheumatoid Arthritis: The RESET-RA Study
Protocol Number	SPM-020
ClinicalTrials.gov Identifier	NCT04539964
Investigational Device	The SetPoint System
Study Sponsor's Name and Address	SetPoint Medical, Inc. 25101 Rye Canyon Loop Valencia, CA 91355
Biostatistics and Data Analysis	SetPoint Medical, Inc.

TABLE OF CONTENTS

LIST OF TABLES

Revision History

Revision	Revision Date	Summary of Changes
A	05MAY2021	Document created
B	29JAN2024	• Updates made for consistency with current revision of CLP-001, Clinical Investigational Protocol SPM-020 (The RESET-RA Study) (p. 7) • Updates made for consistency with current version of CLP-003, Data Monitoring Committee Charter for SPM-020 (The RESET-RA Study) (pp. 7-8) • Added subgroup analyses for subjects receiving augmented therapy (pp. 9, 18, Appendix B pp. 17, 23, 29, 35, 74-77) • Generalized language pertaining to software requirements for statistical analysis (p. 10) • Change in nomenclature from Open-label PTE population to Treatment to Open Label (TOL), and crossover PTE population to Control to Open Label (TOL) for accuracy (p. 10, table and listing headers and footers throughout Appendices B & C) • Removed reference to collecting safety data once a subject is withdrawn from the study (p. 10) • Rescue language and penalty as treatment failures is removed because additional RA treatment is allowed during open-label follow-up per protocol (p. 11) • Added detail on missing analytes/retests (p. 11) • Clarified missing data approaches (p. 12) • Descriptions of ACR components removed as the section is duplicative with CLP-004; CLP-004 is referenced (p. 13) • Added detail on methods for calculating and analyzing RAMRIS scores (p. 16) • Removed information on calculation of SF-36 scores and replaced with reference to the same information which is found in the SF-36 User's Manual (p. 16) • Clarified information on calculation of the EQ-5D-5L score (p. 17, Appendix B, pp. 63-67) • Updated description of how AEs are categorized for consistency with study protocol (p. 18, Appendix B, p. 88) • Added listing of subjects receiving augmented therapy (Appendix C, p. 6)
C	15JUL2024	• Extended study duration by adding 6 visits as part of open-label, long-term follow-up after completion of Week 12 (pp. 7-8, 21)

2 LIST OF ABBREVIATIONS

Abbreviation	Expansion
ACR	American College of Rheumatology
AE	Adverse event
CARLOS	Cartilage Loss Score
CDAI	Clinical Disease Activity Index
CI	Confidence interval
CMO	Chief Medical Officer
COL	Control to Open Label
CRF	Case report form
DAS	Disease Activity Score
DMARD	Disease-modifying antirheumatic drug
DMC	Data monitoring committee
EDC	Electronic data capture
EGA	Evaluator's global assessment
EQ-5D-5L	EuroQol 5 domains 5 levels
EULAR	European League Against Rheumatism
HAQ-DI	Health Assessment Questionnaire Disability Index
hsCRP	High-sensitivity C-reactive protein
IL	Interleukin
IRB	Institutional Review Board
ITT	Intent to treat
JAKi	Janus kinase inhibitors
LDA	Low disease activity
LOCF	Last observation carried forward
MCID	Minimal clinically important difference
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
NRI	Non-responder imputation
NRS	Numerical rating scale

Abbreviation	Expansion
OC	Observed case
PCS	Physical component summary
PD	Protocol deviation
PMA	Premarket Approval
PT	Preferred term
PTE	Per-treatment evaluable
RA	Rheumatoid arthritis
RAMRIS	Rheumatoid Arthritis MRI Scoring System
RF	Rheumatoid factor
SADE	Serious adverse device effect
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Statistical Analysis Software
SD	Standard deviation
SF-36	Short Form Survey with 36 items
SGA	Subject's global assessment
SJC28	Swollen joint count for 28 different joints
SOC	System organ class
SOP	Standard operating procedure
TEAE	Treatment emergent adverse event
TJC28	Tender joint count for 28 different joints
TOL	Treatment to Open Label
UADE	Unanticipated adverse device effect
USADE	Unanticipated serious adverse device effect
WHO	World Health Organization

3 INTRODUCTION

This document outlines the statistical analysis plan (SAP) for the exploratory analysis during the open-label, long-term follow-up period in the RESET-RA study conducted by SetPoint Medical under protocol SPM-020 entitled "Vagus Nerve Stimulation Using the SetPoint System for Moderate to Severe Rheumatoid Arthritis: The RESET-RA Study." The SAP specifies the listings and tabular summaries for the exploratory data analyses to be performed using the data collected during the open-label, long-term follow-up.

Note: The primary, secondary and exploratory efficacy analyses of the randomized, sham-controlled, double-blind data through Week 12 are detailed in a separate SAP (CLP-004).

3.1 Study Objective

The overall objective of this study is to evaluate the safety and efficacy of the SetPoint System for the treatment of adult patients with active, moderate-to-severe RA who have had an inadequate response or intolerance to biologic or targeted synthetic DMARDs.

The specific objective of the open-label follow-up with all subjects receiving active stimulation is to gather long-term safety and exploratory efficacy data.

3.2 Study Design

This is an operationally seamless, 2-stage, randomized, sham-controlled, double-blind, multicenter pivotal study enrolling up to 250 randomized subjects at up to 45 study centers across the U.S. After completing a 12-week follow-up for the primary efficacy endpoint, there is a one-way crossover of the control group and a 252-week follow-up of all subjects on active stimulation for long-term safety and exploratory efficacy data. The blinding to the original treatment assignment will be maintained until the last subject completes Week 12 assessments, and the study dataset for the primary analysis is locked.

3.3 Study Visits and Assessments During Extension

The open-label follow-up will begin after completion of assessments at Week 12 and a one-way crossover of the control group to active stimulation. Subjects receiving active stimulation will continue on active stimulation. Subjects will return for 3 device titration visits (Titration 4, 5 and 6 at Week 13, 14, 15, respectively), and 21 follow-up assessment visits every 12 weeks from Week 24 through Week 264 (end of study). See **Appendix A** for Schedule of Assessments.

4 TYPE OF PLANNED ANALYSES

4.1 DMC Analysis

An independent Data Monitoring Committee (DMC) consisting of external, independent rheumatology, surgery and biostatistics experts will continue to provide ongoing monitoring of the safety, efficacy and overall study conduct. The DMC's role and responsibilities and the scope of

study oversight are detailed in the DMC Charter, which defines the DMC membership, meeting logistics, and meeting frequency.

During long-term extension, once the last study subject has been enrolled, the DMC will continue to meet once every 6 months and provide recommendations for continuing or stopping the study based on their ongoing review of cumulative safety data, including AEs, SAEs, device deficiencies, protocol deviations, and concomitant medications, as well as descriptive summaries of TJC28 and SJC28.

The DMC meetings will be performed in closed sessions until the study is unblinded. Data access is described in **Table 1**

Table 1: Data Access Matrix During Open-Label Extension

Department/Role	Blinded	Unblinded	Note
CEO	B		Receiving DMC recommendations
Clinical Operations[1]	B	--	Not having access to randomization assignments or DMC Closed Session reports to preserve blinding of everyone involved directly or indirectly in the study conduct until locking the study dataset for the primary efficacy analysis at Week 12
Clinical Data Management	B	--	Consultants to sponsor responsible for managing EDC and IRT, generating data exports and not having access to randomization assignments until locking the study dataset for the primary efficacy analysis at Week 12
Study Biostatisticians	B	--	Consultants to sponsor responsible for programming but not having access to randomization assignments until locking the study dataset for the primary efficacy analysis at Week12.
Independent Biostatistician	--	U	Non-voting statistician reporting to DMC responsible for receiving blinded data exports, accessing randomization assignments, conducting unblinded analyses and preparing outputs for review during DMC closed sessions
DMC	--	U	DMC chairperson, biostatistician, and clinicians participating in closed meetings

Abbreviations: B, blinded; CEO, Chief Executive Officer; DMC, data monitoring committee; EDC, electronic data capture; U, unblinded.

[1]Clinical operations includes but is not limited to Chief Medical Officer, Vice President of Clinical Affairs, Managers of Clinical Affairs/Operations, Clinical Research Associates, Field Clinical Engineers.

4.2 Exploratory Analysis

During the open-label follow-up, changes in exploratory efficacy endpoints at Week 24, 48, 96, 144 and 264 (end of study) will be evaluated in comparison to baseline and Day 0 for the treatment population and Week 12 for the crossover population using data for all subjects available at a given timepoint (**Table 2**). Refer to Section **5.2** for definitions of populations.

Table 2: Summary of Exploratory Efficacy Endpoints

Endpoint	Display	TOL	COL	Subgroup
ACR20/50/70 response	T, L	Y	Y	Y [1]
DAS28-CRP moderate/good EULAR response	T, L	Y	Y	Y
DAS28-CRP response (MCID)	T, L	Y	Y	Y
HAQ-DI score change and response (MCID)	T, L	Y	Y	Y
ACR components (TJC28, SJC28, Subject Pain, SGA, HAQ-DI, EGA, hsCRP) 20/50/70response	T, L	Y	Y	--
DAS28-CRP score change, LDA/remission	T, L	Y	Y	--
CDAI score change, LDA/remission, response (MCID)	T, L	Y	Y	--
RAMRIS (bone erosion, osteitis, synovitis, CARLOS) score change, progression (bone erosion) at Week 24	T, L	Y	Y	--
EQ-5D-5L score change	T, L	Y	Y	--
SF-36/PCS/MCS score change	T, L	Y	Y	--
Percent change in inflammatory biomarkers at Week 24	T, L	Y	Y	--
Subject satisfaction at Week 24	T, L	Y	Y	--

Abbreviations: ACR, American College of Rheumatology; CARLOS, cartilage loss score; CDAI, Clinical Disease Activity Index; COL, control to open label; CRP, C-reactive protein; DAS, Disease Activity Score; EGA, evaluator's global assessment; EQ-5d-5L, EuroQol 5 domains 5 levels; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high sensitivity CRP; L, listings; LDA, low disease activity; RAMRIS, Rheumatoid Arthritis MRI Scoring System; SF-36, Short Form Survey with 36 items; SGA, subject's global assessment; T, tables; TJC, tender joint count; TOL, treatment to open label; SJC, swollen joint count; Y, yes.
[1] Subgroup analyses as defined in Section **6.3**

Note: All score values are determined at all timepoints, unless stated otherwise. All response rates are determined based on change from baseline (i.e., on the day of informed consent for OL PTE population and Week 12 for CO PTE population) to a specified timepoint. Refer to Section **5.2** for definitions of populations Sections **6.2** for definition of response for specific endpoints.

5 STATISTICAL METHODS

5.1 General Considerations for Data Analyses

The exploratory analyses and safety evaluations are considered *a priori* analyses because they have been prespecified in the SAP prior to locking the database. All other analyses, if any, designed subsequent to locking the database will be considered *post-hoc* analyses, and their results will be considered exploratory. Any *post hoc* analyses will be clearly identified in the clinical study report.

Continuous data will be summarized in terms of the mean, SD, median, minimum, maximum and number of observations, unless otherwise stated. The minimum and maximum will be reported to the same number of decimal places as the raw data recorded in the database. The mean and median will be reported to 1 more decimal place than the raw data recorded in the database. The SD will be reported to 2 more decimal places than the raw data recorded in the database. In general, the maximum number of decimal places reported shall be 4 for any summary statistic.

Categorical data will be summarized in terms of the number of subjects providing data at the relevant time point, frequency counts and percentages. If not stated otherwise, percentages will be presented with one decimal place. Percentages will not be presented for zero counts. Percentages will be calculated using n as the denominator. 100% will be presented without decimal places.

95% Confidence intervals (CI) will be presented to 1 more decimal place than the raw data. Unless stated otherwise, a two-sided 95% confidence level will be calculated when confidence interval is presented.

Data from the protocol-specified visits (i.e., as reported in CRF) will be used in the summary tables (**Appendix B**) and data listings (**Appendix C**). All report outputs will be produced using a software package widely recognized as acceptable for analyzing clinical data in a secure and validated environment.

5.2 Analysis Populations

Analysis population defines the subjects to be included in an analysis. The exploratory analyses will be conducted on the Treatment to Open Label (TOL) and Control to Open Label (COL) populations. The safety analyses will be evaluated on the safety population. All analysis populations are defined below and the exploratory endpoints summarized in **Table 2**.

- *Treatment to Open Label (TOL):* The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
- *Control to Open Label (COL):* The COL population comprises Control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
- *Safety population*. All enrolled subjects.

5.3 Study Day Calculation

Study day is calculated relative to the date of Day 0 (randomization) and will appear in the listings where applicable. If the date of event is on or after Day 0, study day will be calculated as:

Study day = date of event – date of Day 0 (randomization)

5.4 Change from Baseline Calculation

Percent change from baseline to any time point will be calculated as follows:

$$[\text{Value}_{(\text{Post-baseline})} - \text{Value}_{(\text{Baseline})}] / \text{Value}_{(\text{Baseline})} \times 100$$

A negative value reflects a decrease in a given parameter, while a positive relative difference reflects an increase in the parameter.

5.5 Missing Data

For continuous endpoints, change from baseline will be set to missing at visits with missing values or where data were imputed to missing.

For binary endpoints, subjects with missing efficacy data or early withdrawals will be set to missing.

Additional rules for handling of missing data are detailed below:

- *Missing efficacy data*. Visits with missing data (due to a missed visit or missing component of a composite endpoint) will be set to missing.
- *Early withdrawals*. Visits following the early withdrawal will be set to missing.
- *Missing baseline value.* For efficacy endpoints, a missing value at baseline will not be imputed, and the endpoint will be set to missing for all visits.
- *Missing analytes/ retests*. If an analyte value is missing/ its concentration cannot be reliably determined (eg. sample was lost, damaged, etc.), a retest value will be used for that analyte. If an initial value is non-missing and reliable but the analyte was retested, the value that coincides with the date of clinical assessment will be used. If neither an initial and nor retest value are available, the analyte value will be set to missing.
- For missing dates, refer to **Section 5.8** of CLP-004.

5.5.1 Multiple Assessments and Visits

If a variable (e.g., MRI, TJC, SJC) has been assessed multiple times at the same visit, only the last assessment will be used.

Only completed scheduled visits will be included in summary tables (**Appendix B**). Listings will include scheduled and unscheduled visits (**Appendix C**).

5.6 Data Assurance

All tables, figures and data listings to be included in the report will be independently checked for consistency, integrity and in accordance with the study sponsor's SOPs.

5.7 Coding Dictionaries

AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 21.0 or later). Concomitant medications will be coded using the March 2019 or later version of the WHO Drug Global dictionary.

6 EXPLORATORY EFFICACY ANALYSES

6.1 General Considerations

For each follow-up time point, all dichotomous variables will be reported as responders / patients who have achieved that follow-up duration, percentage of responders, and 95% CI.

Values will be reported at each follow-up timepoint.

For continuous measures, mean, SD, median, minimum and maximum will be presented at each time point.

Time will be measured from initiation of stimulation. Therefore study participants originally randomized to stimulation will, for example, have Week 24 visits represented at 24 weeks of follow-up while study participants randomized to sham will have Week 24 visits represented as 12 weeks, since they will have been on stimulation on for 12 weeks at the Week 24 visit.

6.1.1 Missing endpoint data imputation

Below are the descriptions for the imputation methods that may be used throughout the efficacy analyses:

- *Observed case (OC).* Missing values remain missing. For the categorical composite endpoints, in the case that some components are missing, the composite endpoint assessment will be derived based on the non-missing components. If non-missing components are not sufficient to determine final composite endpoint, then the composite endpoint will be set as missing. For continuous composite endpoints, if any components are missing, the composite endpoints will be set as missing.
- *Last observation carried forward (LOCF).* Baseline and Day 0 measurements will not be carried forward to post-baseline. Only measurements post Day 0 will be LOCF for continuous and binary response measures. For the composite endpoints, the last non-missing, post-Day 0 observation will be carried forward to subsequent visits for each individual component first, and then the composite endpoints using individual components imputed by LOCF will be calculated as described above. If a subject does not have a non-missing observed record for a post-Day 0 visit, the last post-Day 0 record prior to the missed visit will be used. If the last non-missing observation prior to the missing visits cannot be determined due to multiple measurements occurring at the same time or the time not available within the same day, the worst outcome will be used for LOCF. If missing components still exist after LOCF, the composite endpoints will be calculated using the same rules as described in OC.
- *Non-responder imputation (NRI).* For all binary response measurements, starting from OC, all missing will be set as non-responders.

If subject only had baseline measurements, LOCF and OC analyses will not include this subject. But this subject will be treated as non-responder in NRI analyses.

6.2 Clinical Variables

For descriptions and definitions of ACR components (TJC28, SJC28, Subject's Pain Assessment, SGA, EGA, HAQ-DI, hsCRP), refer to Section **8.2** of CLP-004.

6.2.1 ACR20/50/70

A subject achieves ACR20/50/70 response when this subject experiences a ≥ 20%/50%/70%, respectively improvement from baseline to a given timepoint in TJC28, SJC28, and at least 3 of the following 5 items:

- Subject's pain assessment
- SGA
- EGA
- HAQ-DI
- hsCRP

For all visits, if any of the component scores are missing, then those scores will be considered as not having met the criteria for improvement. If 3 or more of the 5 remaining ACR measures are missing, ACR20/50/70 will each be considered missing.

For component scores with missing baseline values or a baseline value of 0, the percentage improvement cannot be calculated, and the component will be considered as not having met the criteria for improvement for all visits.

20/50/70 response for each component (TJC28, SJC28, Subject's Pain Assessment, SGA, HAQ-DI, EGA, hsCRP) corresponds to 20, 50 and 70% improvement from baseline to a given timepoint, respectively.

6.2.2 DAS28-CRP

The Disease Activity Score (DAS) is a derived measurement of 4 components with differential weighting:

- TJC28
- SJC28
- hsCRP (mg/L)
- SGA

A total score ranges from 0 to 10 and is computed as follows:

DAS28-CRP = 0.56 * sqrt(TJC28) + 0.28 * sqrt(SJC28) + 0.36 * ln(CRP+1) + 0.014 * SGA + 0.96

If one of the components is missing at an individual assessment point, the DAS28-CRP value for that assessment will be set to missing. An alternative imputation method for missing components may be applied as described in Section **6.1.1**.

The DAS28-CRP score corresponds to the current RA activity:

- 0 to < 2.6 Remission
- 2.6 to < 3.2 Low disease activity (LDA)
- 3.2 to ≤ 5.1 Moderate activity
- > 5.1 High activity

A DAS28-CRP score reduction by 1.2 represents the MCID.

6.2.3 DAS28-CRP Good/Moderate EULAR Response

DAS28-CRP good/moderate EULAR response is defined based on the combination of the current DAS28-CRP score and its improvement relative to baseline as illustrated in **Table 3**.

A subject is considered having a moderate treatment response if:

- DAS28-CRP score improvement from baseline to a given timepoint is > 0.6 and ≤ 1.2, and the DAS28-CRP score at that timepoint is ≤ 5.1; or
- DAS28-CRP score improvement from baseline to a given timepoint is > 1.2, and the DAS28-CRP score at that timepoint is > 3.2.

A subject is considered having a good treatment response if:

- DAS28-CRP score improvement from baseline to a given timepoint is > 1.2 and the DAS28-CRP score at that timepoint is ≤ 3.2.

Table 3: EULAR Response Criteria

DAS28-CRP Score at a Given Timepoint	DAS28-CRP Score Decrease from Baseline Value to a Given Timepoint		
	> 1.2	**> 0.6 to ≤ 1.2**	**≤ 0.6**
≤ 3.2	Good response	Moderate response	No response
> 3.2 to ≤ 5.1	Moderate response	Moderate response	No response
> 5.1	Moderate response	No response	No response

If the post-baseline DAS28-CRP score is missing, then the corresponding EULAR category will be missing.

Missing DAS28-CRP values will be set as missing.

6.2.4 CDAI

The Clinical Disease Activity Index (CDAI) is a composite score consisting of the sum of:

- SJC28
- TJC28
- SGA/10
- EGA/10

The CDAI score is calculated as follows and ranges from 0 to 76 with higher values representing higher disease activity:

CDAI = TJC28 + SJC28 + SGA + EGA

The CDAI score corresponds to the current RA activity:

- 0 to ≤ 2.8 Remission
- >2.8 to ≤ 10 Low disease activity (LDA)
- >10 to ≤ 22 Moderate activity
- > 22 High activity

The MCID varies depending on RA activity at baseline:

- -12 for high activity
- -6 for moderate activity
- 1 for low activity

If one of the components is missing at a given assessment point, no imputations will be done, and the CDAI value for that assessment will be set to missing. An alternative imputation method for missing components may be applied as described in Section **6.1.1**.

6.2.5 RAMRIS

RAMRIS is the standardized system for RA MRI scoring of 4 different types of joint pathologies in the wrist and the hand. A total score for each pathology is generated by the summation of individual joint/bone scores as follows:

- *Synovitis*. 8 joints each scored on a scale from 0 = normal to 3 = severe, resulting in a total score from 0 to 24.
- *Bone erosion*. 25 bones each scored on a scale from 0 to 10, resulting in a total score from 0 to 250. An increase of > 0.5 from baseline to Week 12 will represent disease progression.
- *Osteitis*. 25 bones scored on a scale from 0 to 3, resulting in a total score from 0 to 75.

- *CARLOS (cartilage loss).* 25 joints each scored on a scale from 0 to 4, resulting in a total score from 0 to 100.

Subjects will undergo MRI at Week 24, and the MRI images will be scored by the same independent centralized blinded readers who scored baseline and Week 12 MRIs. Scores for each bone/joint will be calculated as the average of the score provided by each of the two readers. If a RAMRIS score from one of the readers is missing, then the RAMRIS score from the other reader will be used. If the score was missing for both readers at any given time point, the average score is considered missing. An imputation method for missing components may be applied as described in Section **6.1.1**.

The smallest detectable change (SDC) will be calculated for each of the joint pathologies to assess whether a patient experienced a change beyond measurement error. The SDC is calculated as:

$$\pm 1.96 \times SD_{\Delta(\text{CHANGE SCORES})} / (\sqrt{2} \times \sqrt{k})$$

where CHANGE SCORE = change in RAMRIS total score between two timepoints, $SD_{\Delta(\text{CHANGESCORES})}$ represents the standard deviation of difference in change scores between the two readers, and k= the number of readers (Bruynesteyn et al., 2005).

In addition, subgroup analyses will be performed for subjects with and without baseline joint damage that is predictive of future progression (Gandjbakhch et al, 2014).

6.2.6 SF-36

Health-related quality of life will be assessed using the subject-completed Medical Outcomes Study Short-Form 36 (SF-36), which is a generic health survey that contains 36 questions covering eight domains of health. The SF-36 yields an 8-scale profile of functional health and well-being scores as well as physical and mental component health summary scores. The version 2, 4-week recall questionnaire will be used. Recoding, calculations and standardization will be done as recommended in the User's manual for the SF-36 (Mariush, 2011). Each of the 8 domain scores is the sum of some of the overall 36 item scores.

The initial domain scores are the sum of individual item scores:

- General Health
- Physical Functioning
- Role Physical
- Role Emotional
- Social Functioning
- Bodily Pain
- Vitality

- Mental Health

Domain scores will only be calculated if less than half of the item scores are missing. An imputation method for missing components may be applied as described in Section **5.5.1**.

6.2.7 EQ-5D-5L

A standardized instrument for measuring general health status within the following 5 dimensions:

- Mobility
- Self-care
- Usual activities
- Pain/discomfort
- Anxiety/depression

Each dimension is scored on 5-point scale as:

- 1 = No problems
- 2 = Slight problems
- 3 = Moderate problems
- 4 = Severe problems
- 5 = Extreme problems

General health status is scored on a VAS (0 = poor to 100 = the best). An imputation method for missing components may be applied as described in Section **5.5.1.**

Reduction in the proportion of subjects with problems (moderate, severe or extreme) will represent improvement.

An EQ-5D summary index score can be derived by applying a formula that attaches weights, or index values, to each of the levels in each dimension. The index is calculated by deducting the appropriate weights from the value for full health (i.e., 1). Value sets are country specific and can be obtained from the EuroQol website (EuroQol Research Foundation, 2023).

6.3 Subgroup Analyses

Response rates for the key exploratory efficacy endpoints, as specified in **Table 2**, will be examined using the following subgroups:

- Number of prior biologic and targeted synthetic DMARDs (e.g., < 4 vs. ≥ 4)
- Prior use of JAKi (Yes vs. No)
- RA activity at baseline (DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1)

- RA severity at imitation of stimulation (< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28)
- Augmented therapy (yes, no)

After completion of Week 12 assessments, additional treatment for RA may be provided at any time. The decision about the need, type and timing of treatment is left to the discretion of the Co-PI Rheumatologist and the subject. The initiation of these treatments with study treatment during open-label follow-up is considered "augmented therapy". Subjects combining stimulation with the following additions to RA therapy will fall into the augmented therapy subgroup for analysis of response rates for key exploratory efficacy endpoints at specific timepoints:

- *Prednisone equivalent >10 mg/day.* If average daily corticosteroid use exceeds 10 mg/day prednisone after a period (time from previous visit up to the day before the current visit), the subject is assigned to the augmented therapy subgroup for that visit.
- *Corticosteroid injection.* If subject received a corticosteroid injection within 30 days prior to a study visit, the subject is assigned to the augmented therapy subgroup for that visit.
- *b/ts/csDMARD.* Subjects who receive treatment with biologic, targeted synthetic, or additional conventional synthetic DMARD, or increased dose of background conventional synthetic DMARD will be assigned to the augmented therapy subgroup for all subsequent visits.

7 SAFETY EVALUATION

7.1 AE and SAEs

The incidence of AEs and SAEs in the safety population (see Section **5.2**) will be tabulated through Week 264 (end of study). Each AE will be evaluated by clinical investigators in terms of seriousness, severity (i.e., mild, moderate, severe) and strength of relationship (i.e., not related, unlikely related, probably related, definitely related, indeterminate) to the implant procedure, explant procedure, implant device, stimulation and Energizer. Any AE that is determined by a participating investigator to be related (definitely related or probably related) to the implant procedure, explant procedure, implant device, stimulation or Energizer will be categorized as device related.

For all AE tables, a subject reporting the same adverse event more than once will be counted once when calculating the number and percentage of subjects with that particular event. If a subject reports the same AE more than once or has the same AE on multiple occasions, the maximum severity grade and relationship to the study implant and/or study drug will be presented.

The frequencies and percentages of treatment-emergent adverse events will be presented by MedDRA system organ class (SOC) and preferred term (PT). Complete subject listings of all AE will be provided. For each AE the following will be specified: start and stop dates, severity grade, MedDRA SOC and PT, relationship (unlikely related, probably related, definitely related or indeterminate) to the implant procedure, explant procedure, implant device, stimulation or Energizer , and, as well as action taken, outcome of the adverse event, and seriousness.

7.2 Protocol Deviations

All protocol deviations will be tabulated with reasons for deviations reviewed by sponsor and reported in compliance with the study protocol, IRB requirements and sponsor's SOPs.

Summary tables with the number and percentage of subjects with protocol deviations will be provided by type of deviation (**Appendix B**). A by-subject listing of all protocol deviations will be provided (**Appendix C**).

7.3 Device Deficiencies

All device deficiencies related to the identity, quality, durability, reliability, safety or performance of the study device, including device malfunctions, use errors, and inadequate labelling will be tabulated. Summary tables with the number and percentage of device deficiencies will be provided by type (**Appendix B**). A by-subject listing of all device malfunctions will be provided (**Appendix C**).

8 STATISTICAL CONSIDERATIONS RELATED TO COVID-19

The statistical considerations detailed in this section are consistent with the FDA's guidance on the conduct of clinical trials during the COVID-19 pandemic and recommendations for the statistical analysis of the primary and key secondary endpoints to help ensure that the COVID-19-related changes to the RESET-RA study conduct will provide interpretable findings with correct statistical quantification of uncertainty.

8.1 Impact of COVID-19 on Study Integrity

Unavoidable protocol modifications may be required due to COVID-19 illness and/or COVID-19 control measures to protect subject safety and the to address its impact on the ability to collect data. The context and/or reasons for post-baseline events as they relate to COVID-19, such as discontinuation of treatment, withdrawal from the trial, use of alternative or rescue treatments, missed endpoint assessments, and the use of alternative endpoint assessment methods will be captured at the subject level. Information not specific to individual subjects, such as information on site closure (rheumatology or surgery) and its impact on disrupting administration of the investigational study device (i.e., implant procedure, device titration, device adjustments) will also be captured. This information at both the subject and site levels may be useful for incorporating into additional sensitivity analyses related to the impact of COVID-19.

8.2 COVID-19 Analysis Considerations

The impact of COVID-19 on the study integrity will be assessed and included into data summaries, including information on missing data, protocol deviations, subject discontinuation or interruption of the investigational treatment, subject withdrawal, and changes in endpoint assessments (e.g., virtual visit).

Extending the protocol-defined windows and using alternative remote methods for assessment of the exploratory efficacy endpoints may be warranted to address the impact of COVID-19. The data

from these late or modified assessments can be leveraged based on scientifically based rationale and clinical judgement.

The available data at baseline and post-baseline, including COVID-19-related information will be leveraged using the prespecified methods for handling missing data.

9 REFERENCES

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10 APPENDICES

Appendix A: Schedule of Assessments

Assessment	Titration 4 (91 ± 2d[2])	Titration 5 (98 ± 2d[2])	Titration 6 (105 ± 2d[2])	Week 24 (168 ± 7d[2])	Week 36 (252 ± 14d[2])	Week 48 (336 ± 14d[2])	Week 60 (420 ± 14d[2])	Week 72 (504 ± 14d[2])	Week 84 (588 ± 14d[2])	Week 96 (672 ± 14d[2])	Week 108 (756 ± 14d[2])	Week 120 (840 ± 14d[2])	Week 132 (924 ± 14d[2])	Week 144 (1,008 ± 14d[2])	Week 156 (1,092 ± 14d[2])	Week 168 (1,176 ± 14d[2])	Week 180 (1,260 ± 14d[2])	Week 192 (1,344 ± 14d[2])	Week 204 (1,428 ± 14d[2])	Week 216 (1,512 ± 14d[2])	Week 228 (1,596 ± 14d[2])	Week 240 (1,680 ± 14d[2])	Week 252 (1,764± 14d[2])	Week 264 (1,848 ± 14d[2]) (End of Study)
Vital signs				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (childbearing female)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
RA disease activity assessments[1]				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SF-36 & EQ-5D-5L questionnaires				X		X				X				X				X						
Satisfaction questionnaire				X																				
Blood collection (CBC)				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood collection (biomarkers)				X																				
Hand MRI				X																				
12-lead ECG				X		X				X				X				X						
Device check & dose titration	X[3]	X[3]	X[3]																					
Device check & dose adjustment if needed				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Device deficiency reporting	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse event reporting	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Abbreviations: CBC, complete blood count; d, day; EGA, evaluator's global assessment; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging; RA, rheumatoid arthritis; SGA, subject's global assessment; SJC, swollen joint count; TJC, tender joint count.

[1] RA disease activity assessments include: HAQ-DI, SGA, subject's pain assessment, TJC28, SJC28, EGA, and hsCRP. Subjects must have ≥ 4TJC28 and ≥ 4SJC28 at consent to be eligible.
[2] From Day 0 (randomization).
[3] Dose titration is not performed if subject and Co-PI Rheumatologist decide that subject should not receive active stimulation in open-label, long-term follow-up period.

Appendix B: Table Mockups

Table 14.8.1.1
Subject Disposition

	TOL [1]	COL [2]	Overall
Number of subjects:			
TOL [1]	xxx	--	--
COL [2]	--	xxx	--
Overall population	--	--	xxx
Withdrawn	xxx	xxx	xxx
Completed study through Week 192	xxx	xxx	xxx
Primary reason for withdrawal [3]:			
Subject decision to withdraw consent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Investigator decision or medical judgement	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Lost to follow-up	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Device malfunction	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Adverse event	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subject no longer eligible	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Death	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Study terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Sponsor or IRB decision	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Abbreviations: COL, Control to Open Label; ITT, intent to treat; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL, Overall).

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Table 14.8.1.2
Demographic and Baseline Characteristics

	TOL [1]	COL[2]	Overall [3]
N	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Age (years)			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.xx	xx.xx	xx.xx
Min-Max	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
Gender [3]			
Male	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Female	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Ethnicity [3]			
Hispanic or Latino	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Hispanic or Latino	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not disclosed	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Race [3][4]			
American Indian or Alaska Native	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Asian	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Black or African American	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Native Hawaiian or other Pacific Islander	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
White	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
RA duration (years) [3]			
N	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.xx	xx.xx	xx.xx
Min-Max	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
BMI (kg/m^2)			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx

	TOL [1]	COL[2]	Overall [3]
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
RF [3]			
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ACPA [3]			
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for RF and/or ACPA [3]			
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
hsCRP (mg/L)			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
TJC28			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SJC28			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
CDAI score			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
DAS28-CRP score			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)

	TOL [1]	COL[2]	Overall [3]
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
HAQ-DI score			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
EQ-5D-5L Index			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
EQ-VAS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SF-36 MCS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
SF-36 PCS			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
Number of prior b/ts DMARDs			
N	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x

	TOL [1]	COL[2]	Overall [3]
Number of prior b/ts DMARDs [3]			
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4			
5			
6			
7			
8			
9			
10+			
Prior b/ts DMARDs [3]			
Anti-IL-1 agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anti IL-6 agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anti-TNF agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
B-cell depleting agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
JAKi	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CTLA4-Ig	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Abbreviations: ACPA, anti-citrullinated protein antibodies; b/tsDMARD, biologic or targeted synthetic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; COL, Control to Open Label; CTLA4-Ig, cytotoxic T-lymphocyte-associated antigen-4 immunoglobulin; DAS, Disease Activity Score; eGFR, estimated glomerular filtration rate; EQ-5D-5L Index, EuroQol-5D-5L Index; EQ-VAS, EuroQol Visual Analogue Scale; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high-sensitivity C-reactive protein; IL, interleukin; ITT, intent to treat; JAKi, Janus Kinase inhibitor; OL, open label; PTE, per-treatment-evaluable; RF, rheumatoid factor; SD, standard deviation; SJC, swollen joint count; SF-36 MCS, Short Form 36 Mental Component Summary Score; SF-36 PCS, Short Form 36 Physical Component Score; TJC, tender joint count; TNF, tumor necrosis factor*; TOL, Treatment to Open Label*

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL, Overall).
[4] Race selected based on all that applied.

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.1
ACR20/50/70 Response

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
ACR20 response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
ACR20 response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
ACR50 response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
ACR50 response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
ACR70 Response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 192		
ACR70 response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; COL, Control to Open Label; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.1.1
Subgroup Analysis of ACR20 Response: Prior b/tsDMARDs

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
ACR20 response from baseline [4]		
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
ACR20 response from initiation of stimulation [5]		
Prior b/tsDMARD < 4		
Week 24		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD > 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; COL, Control to Open Label; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.1.1.1
Subgroup Analysis of ACR50 Response: Prior b/tsDMARDs

Repeat Table 14.8.2.1.1 for ACR50

Table 14.8.2.1.1.2
Subgroup Analysis of ACR70 Response: Prior b/tsDMARDs

Repeat Table 14.8.2.1.1 for ACR70

Table 14.8.2.1.2
Subgroup Analysis of ACR20 Response: Prior JAKi

Repeat Table 14.8.2.1.1 for Prior JAKi [Yes vs. No]

Add to abbreviations: *JAKi, Janus kinase inhibitor*.

Table 14.8.2.1.2.1
Subgroup Analysis of ACR50 Response: Prior JAKi

Repeat Table 14.8.2.1.1 for ACR50 and for Prior JAKi [Yes vs. No]

Table 14.8.2.1.2.2
Subgroup Analysis of ACR70 Response: Prior JAKi

Repeat Table 14.8.2.1.1 for ACR70 and for Prior JAKi [Yes vs. No]

Table 14.8.2.1.3
Subgroup Analysis of ACR20 Response: RA Activity at Baseline

Repeat Table 14.8.2.1.1 for RA Disease Activity at Baseline [DAS28-CRP ≤ 5.1 vs DAS28-CRP > 5.1]

Add to abbreviations: *DAS, Disease Activity Score.*

Table 14.8.2.1.3.1
Subgroup Analysis of ACR50 Response: RA Activity at Baseline

Repeat Table 14.8.2.1.1 for ACR50 and RA Disease Activity at Baseline [DAS28-CRP ≤ 5.1 vs DAS28-CRP > 5.1]

Table 14.8.2.1.3.2
Subgroup Analysis of ACR70 Response: RA Activity at Baseline

Repeat Table 14.8.2.1.1 for ACR70 and for RA Disease Activity at Baseline [DAS28-CRP ≤ 5.1 vs DAS28-CRP > 5.1]

Table 14.8.2.1.4
Subgroup Analysis of ACR20 Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.1.1 for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count.*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.1.4.1
Subgroup Analysis of ACR50 Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.1.1 for ACR50 and for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count.*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.1.4.2
Subgroup Analysis of ACR70 Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.1.1 for ACR70 and for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count.*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.1.5
Subgroup Analysis of ACR20 Response: RA Augmented Therapy

Repeat Table 14.8.2.1.1 for ACR20 and RA Augmented Therapy [yes/no]

Table 14.8.2.1.5.1
Subgroup Analysis of ACR50 Response: RA Augmented Therapy

Repeat Table 14.8.2.1.1 for ACR50 and RA Augmented Therapy [yes/no]

Table 14.8.2.1.5.2
Subgroup Analysis of ACR70 Response: RA Augmented Therapy

Repeat Table 14.8.2.1.1 for ACR70 and RA Augmented Therapy [yes/no]

Table 14.8.2.2
DAS28-CRP Moderate/Good EULAR Response

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
DAS28-CRP moderate/good EULAR response from baseline [4]		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP moderate/good EULAR response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label (COL): DAS, Disease Activity Score; EULAR, European League Against Rheumatism; hsCRP, High-sensitivity C-reactive protein; TOL, Treatment to Open Label (TOL)

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.2.1
Subgroup Analysis EULAR Response: Prior b/tsDMARDs

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
DAS28-CRP moderate/severe EULAR response from baseline [4]		
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP moderate/severe EULAR response from initiation of stimulation [5]		
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; DAS, Disease Activity Score; EULAR, European League Against Rheumatism; hsCRP, High-sensitivity C-reactive protein; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.2.2
Subgroup Analysis of EULAR Response: Prior JAKi

Repeat Table 14.8.2.2.1 for Prior JAKi [Yes vs. No]

Add to abbreviations: *JAKi, Janus kinase inhibitor*.

Table 14.8.2.2.3
Subgroup Analysis of EULAR Response: RA Activity at Baseline

Repeat Table 14.8.2.2.1 for RA Disease Activity at Baseline [DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1]

Add to abbreviations: *DAS, Disease Activity Score.*

Table 14.8.2.2.4
Subgroup Analysis of EULAR Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.2.1 for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.2.5
Subgroup Analysis of EULAR Response: RA Augmented Therapy

Repeat Table 14.8.2.2.1 for RA Augmented Therapy [yes, no]

Table 14.8.2.3
DAS28-CRP MCID Response

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
DAS28-CRP response (MCID ≥ -1.2) from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP response (MCID ≥ -1.2) from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; DAS, Disease Activity Score; CRP, C-reactive protein; MCID, minimal clinically important difference OL, TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.3.1
Subgroup Analysis DAS28-CRP MCID Response: Prior b/tsDMARDs

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
DAS28-CRP response (MCID ≥ -1.2) from baseline [4]		
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP Response (MCID ≥ -1.2) from initiation of stimulation [5]		
Prior b/tsDMARD < 4		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; DAS, Disease Activity Score; CRP, C-reactive protein; MCID, minimal clinically important difference; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL Reference: Listing 16.x.x.x SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}		

Table 14.8.2.3.2
Subgroup Analysis of DAS28-CRP MCID Response: Prior JAKi

Repeat Table 14.8.2.3.1 for Prior JAKi [Yes vs. No]

Add to abbreviations: *JAKi, Janus kinase inhibitor*.

Table 14.8.2.3.3
Subgroup Analysis of DAS28-CRP MCID Response: RA Activity at Baseline

Repeat Table 14.8.2.3.1 for RA Activity at Baseline [DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1]

Add to abbreviations: *DAS, Disease Activity Score.*

Table 14.8.2.3.4
Subgroup Analysis of DAS28-CRP MCID Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.3.1 for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.3.5
Subgroup Analysis of DAS28-CRP MCID Response: Augmented Therapy

Repeat Table 14.8.2.3.1 for RA Augmented Therapy [yes, no]

Table 14.8.2.4
HAQ-DI MCID Response

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
HAQ-DI response (MCID ≥ -0.22) from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
HAQ-DI response (MCID ≥ -0.22) from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; HAQ-DI, Health Assessment Questionnaire Disability Index; MCID, minimal clinically important difference; TOL, Treatment to Open Label;

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.4.1
Subgroup Analysis HAQ-DI MCID Response: Prior b/tsDMARDs

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
HAQ-DI response (MCID ≥ -0.22) from baseline [4]		
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
HAQ-DI response (MCID ≥ -0.22) from initiation of stimulation [5]		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Prior b/tsDMARD < 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Prior b/tsDMARD ≥ 4		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; HAQ-DI, Health Assessment Questionnaire Disability Index; MCID, minimal clinically important difference; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)

[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.4.2
Subgroup Analysis of HAQ-DI MCID Response: Prior JAKi

Repeat Table 14.8.2.4.1 for Prior JAKi [Yes vs. No]

Add to abbreviations: *JAKi, Janus kinase inhibitor*.

Table 14.8.2.4.3
Subgroup Analysis of HAQ-DI MCID Response: RA Disease Activity at Baseline

Repeat Table 14.8.2.4.1 for RA Disease Activity at Baseline [DAS28-CRP ≤ 5.1 vs. DAS28-CRP > 5.1]

Add to abbreviations: *DAS, Disease Activity Score.*

Table 14.8.2.4.4
Subgroup Analysis of HAQ-DI MCID Response: RA Severity at Initiation of Stimulation

Repeat Table 14.8.2.4.1 for RA Severity at Initiation of Stimulation [< 4 TJC28 or < 4 SJC28 vs. ≥ 4 TJC28 and ≥ 4 SJC28]

Add to abbreviations: *TJC, tender joint count; SJC, swollen joint count*

Programming note: For this analysis, remove the "from baseline" portion of the table.

Table 14.8.2.4.5
Subgroup Analysis of HAQ-DI MCID Response: Augmented Therapy

Repeat Table 14.8.2.4.1 for RA Augmented Therapy [yes, no]

Table 14.8.2.5
TJC28

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
TJC28 Score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 192		
TJC28 20% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 50% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 70% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 change from initiation of stimulation		
Day of Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 20% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 50% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
TJC28 70% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Repeat for: Week 36 Week 48 Week 60 Week 72 Week 84 Week 96 Week 108 Week 120 Week 132 Week 144 Week 156 Week 168 Week 180 Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; TJC, tender joint count; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.6
SJC28

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
SJC28 Score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 192		
SJC28 20% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 50% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 70% response from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 change from initiation of stimulation		
Day of Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 20% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 50% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
SJC28 70% response from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Repeat for: Week 36 Week 48 Week 60 Week 72 Week 84 Week 96 Week 108 Week 120 Week 132 Week 144 Week 156 Week 168 Week 180 Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; SJC, swollen joint count; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.7
Subject's Assessment of Pain

Repeat 14.8.2.6 for Subject's Pain Assessment

Note to Programmer: Remove SJC from footnote.

Table 14.8.2.8
SGA

Repeat 14.8.2.6 for SGA

Note to Programmer: Remove SJC from footnote and add *SGA, subject's global assessment*.

Table 14.8.2.9
EGA

Repeat 14.8.2.6 for EGA

Note to Programmer: Remove SJC from footnote and add *EGA, evaluator's global assessment.*

Table 14.8.2.10
hsCRP

Repeat 14.8.2.6 for hsCRP (mg/mL)

Note to Programmer: Remove SJC from footnote and add *hsCRP, high sensitivity C-reactive protein*.

Table 14.8.2.11
DAS28-CRP

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
DAS28-CRP Score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 180		
Week 192		
DAS28-CRP low disease activity (score 2.6 to < 3.2)		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP remission (score 0 to < 2.6)		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
DAS28-CRP score change from initiation of stimulation [5]		
Day of initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 168		
Week 180		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; CRP, C-reactive protein; DAS, Disease Activity Score; TOL, Treatment to Open Label;

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.12
CDAI

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
CDAI score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 180		
Week 192		
CDAI low disease activity (score >2.8 to ≤ 10)		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
CDAI remission (score 0 to ≤ 2.8)		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
CDAI score change from initiation of stimulation [5]		
Day of initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 168		
Week 180		
Week 192		
CDAI response (MCID) from baseline [4]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		
CDAI response (MCID) from initiation of stimulation [5]		
Week 24		
N	xx	xx
Yes [3]	xx (xx.x%)	xx (xx.x%)
95% CI	(xx.x%, xx.x%)	(xx.x%, xx.x%)
Repeat for:		
Week 36		
Week 48		
Week 60		
Week 72		

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 84		
Week 96		
Week 108		
Week 120		
Week 132		
Week 144		
Week 156		
Week 168		
Week 180		
Week 192		

Abbreviations: CDAI, Clinical Disease Activity Index; CI, confidence interval; COL, Contol to Open Label; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.13
RAMRIS

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
RAMRIS bone erosion score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4] (SDC: x.xx)		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Progression rate from baseline (> 0.5)		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
RAMRIS osteitis score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4] (SDC: x.xx)		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
RAMRIS CARLOS score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4] (SDC: x.xx)		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)

Abbreviations: CARLOS, cartilage loss score; CI, confidence interval; COL, Control to Open Label; RAMRIS, Rheumatoid Arthritis MRI Scoring System; SDC, Smallest Detectable Change; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.14
EQ-5D-5L

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
EQ-5D-5L Index score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		
EQ-5D-5L Mobility Dimension		
Baseline [4]		
Level 1 (No problem)	xx (xx.x%)	xx (xx.x%)
Level 2 (Slight problems)	xx (xx.x%)	xx (xx.x%)
Level 3 (Moderate problem)	xx (xx.x%)	xx (xx.x%)
Level 4 (Severe problems)	xx (xx.x%)	xx (xx.x%)
Level 5 (Extreme problems)	xx (xx.x%)	xx (xx.x%)

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
Initiation of stimulation [5]		
Level 1 (No problem)	xx (xx.x%)	xx (xx.x%)
Level 2 (Slight problems)	xx (xx.x%)	xx (xx.x%)
Level 3 (Moderate problems)	xx (xx.x%)	xx (xx.x%)
Level 4 (Severe problems)	xx (xx.x%)	xx (xx.x%)
Level 5 (Extreme problems)	xx (xx.x%)	xx (xx.x%)
Week 24		
Level 1 (No problem)	xx (xx.x%)	xx (xx.x%)
Level 2 (Slight problems)	xx (xx.x%)	xx (xx.x%)
Level 3 (Moderate problems)	xx (xx.x%)	xx (xx.x%)
Level 4 (Severe problems)	xx (xx.x%)	xx (xx.x%)
Level 5 (Extreme problems)	xx (xx.x%)	xx (xx.x%)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		
Repeat for other dimensions:		
EQ-5D-5L Self-care		
EQ-5D-5L Usual activities		
EQ-5D-5L Pain/discomfort		
EQ-5D-5L Anxiety/depression		
EQ-5D-5L Index score		
Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		
EQ-5D-5L VAS score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		

Variable	TOL [1] (N=xxx)	COL[2] (N=xxx)
EQ-5D-5L VAS score		
Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		

Abbreviations: CI, confidence interval; COL, Control to Open Label; EQ-5d-5L, EuroQol 5 domains 5 levels; OL, open label; TOL, Treamtent to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.15
SF-36

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
SF-36 MCS score		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		
Repeat for:		
SF-36 PCS score		
SF-36 MCS score		
Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
Week 48		
Week 96		
Week 144		
Week 192		
Repeat for:		
SF-36 PCS score		

Abbreviations: CI, confidence interval; COL Control to Open Label; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Short Form Survey with 36 items; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.16
Subject Satisfaction

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
How satisfied are you with the SetPoint System for treatment of RA?		
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Very satisfied	xx (xx.x%)	xx (xx.x%)
Satisfied	xx (xx.x%)	xx (xx.x%)
Neither satisfied nor dissatisfied	xx (xx.x%)	xx (xx.x%)
Somewhat dissatisfied	xx (xx.x%)	xx (xx.x%)
Very dissatisfied	xx (xx.x%)	xx (xx.x%)
Would you recommend the SetPoint System to a family member or a friend?		
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Yes	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)

Abbreviations: COL, Control to Open Label; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.17
Inflammatory Biomarkers

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
IL-6 (pg/mL)		
Baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Change from baseline [4]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:		
SAA (µg/mL)		
MMP-3 (pg/mL)		
IL-6 (pg/mL)		
Initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
Week 24		
Change from initiation of stimulation [5]		
N [3]	xx (xx.x%)	xx (xx.x%)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.xx	xxx.xx
Min-Max	xxx.x – xxx.x	xxx.x – xxx.x
95% CI	(xx.x, xx.x)	(xx.x, xx.x)

Repeat for:
SAA (µg/mL)
MMP-3 (pg/mL)

Abbreviations:COL, Control to Open Label; IL, interleukin; MMP, matrix metalloproteinase; SAA, serum amyloid A; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Baseline on the day of informed consent for TOL and Week 12 for COL
[5] Initiation of stimulation at Day 0 for TOL and Week 12 for COL

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.18
RA Augmented Therapy

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Received any RA augmented therapy		
Yes [3]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [4]	xxx (xx.x%)	xxx (xx.x%)
Titration 4	xxx (xx.x%)	xxx (xx.x%)
Titration 5	xxx (xx.x%)	xxx (xx.x%)
Titration 6	xxx (xx.x%)	xxx (xx.x%)
Week 24	xxx (xx.x%)	xxx (xx.x%)
Week 36	xxx (xx.x%)	xxx (xx.x%)
Week 48	xxx (xx.x%)	xxx (xx.x%)
Week 60	xxx (xx.x%)	xxx (xx.x%)
Week 72	xxx (xx.x%)	xxx (xx.x%)
Week 84	xxx (xx.x%)	xxx (xx.x%)
Week 96	xxx (xx.x%)	xxx (xx.x%)
Week 108	xxx (xx.x%)	xxx (xx.x%)
Week 120	xxx (xx.x%)	xxx (xx.x%)
Week 132	xxx (xx.x%)	xxx (xx.x%)
Week 144	xxx (xx.x%)	xxx (xx.x%)
Week 156	xxx (xx.x%)	xxx (xx.x%)
Week 168	xxx (xx.x%)	xxx (xx.x%)
Week 180	xxx (xx.x%)	xxx (xx.x%)
Week 192	xxx (xx.x%)	xxx (xx.x%)
Received csDMARD for RA		
Yes [3]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [4]		
Titration 4	xxx (xx.x%)	xxx (xx.x%)
Titration 5	xxx (xx.x%)	xxx (xx.x%)
Titration 6	xxx (xx.x%)	xxx (xx.x%)
Week 24	xxx (xx.x%)	xxx (xx.x%)
Week 36	xxx (xx.x%)	xxx (xx.x%)
Week 48	xxx (xx.x%)	xxx (xx.x%)
Week 60	xxx (xx.x%)	xxx (xx.x%)
Week 72	xxx (xx.x%)	xxx (xx.x%)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Week 84	xxx (xx.x%)	xxx (xx.x%)
Week 96	xxx (xx.x%)	xxx (xx.x%)
Week 108	xxx (xx.x%)	xxx (xx.x%)
Week 120	xxx (xx.x%)	xxx (xx.x%)
Week 132	xxx (xx.x%)	xxx (xx.x%)
Week 144	xxx (xx.x%)	xxx (xx.x%)
Week 156	xxx (xx.x%)	xxx (xx.x%)
Week 168	xxx (xx.x%)	xxx (xx.x%)
Week 180	xxx (xx.x%)	xxx (xx.x%)
Week 192	xxx (xx.x%)	xxx (xx.x%)
Received b/tsDMARDs for RA [1]		
Yes [3]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [4]		
Titration 4	xxx (xx.x%)	xxx (xx.x%)
Titration 5	xxx (xx.x%)	xxx (xx.x%)
Titration 6	xxx (xx.x%)	xxx (xx.x%)
Week 24	xxx (xx.x%)	xxx (xx.x%)
Week 36	xxx (xx.x%)	xxx (xx.x%)
Week 48	xxx (xx.x%)	xxx (xx.x%)
Week 60	xxx (xx.x%)	xxx (xx.x%)
Week 72	xxx (xx.x%)	xxx (xx.x%)
Week 84	xxx (xx.x%)	xxx (xx.x%)
Week 96	xxx (xx.x%)	xxx (xx.x%)
Week 108	xxx (xx.x%)	xxx (xx.x%)
Week 120	xxx (xx.x%)	xxx (xx.x%)
Week 132	xxx (xx.x%)	xxx (xx.x%)
Week 144	xxx (xx.x%)	xxx (xx.x%)
Week 156	xxx (xx.x%)	xxx (xx.x%)
Week 168	xxx (xx.x%)	xxx (xx.x%)
Week 180	xxx (xx.x%)	xxx (xx.x%)
Week 192	xxx (xx.x%)	xxx (xx.x%)
Received corticosteroids (equivalent >10mg/day mean dose prednisone) for RA		
Yes [3]	xxx (xx.x%)	xxx (xx.x%)
If yes, first noted at [4]		
Titration 4	xxx (xx.x%)	xxx (xx.x%)

Variable	TOL [1] (N=xxx)	COL [2] (N=xxx)
Titration 5	xxx (xx.x%)	xxx (xx.x%)
Titration 6	xxx (xx.x%)	xxx (xx.x%)
Week 24	xxx (xx.x%)	xxx (xx.x%)
Week 36	xxx (xx.x%)	xxx (xx.x%)
Week 48	xxx (xx.x%)	xxx (xx.x%)
Week 60	xxx (xx.x%)	xxx (xx.x%)
Week 72	xxx (xx.x%)	xxx (xx.x%)
Week 84	xxx (xx.x%)	xxx (xx.x%)
Week 96	xxx (xx.x%)	xxx (xx.x%)
Week 108	xxx (xx.x%)	xxx (xx.x%)
Week 120	xxx (xx.x%)	xxx (xx.x%)
Week 132	xxx (xx.x%)	xxx (xx.x%)
Week 144	xxx (xx.x%)	xxx (xx.x%)
Week 156	xxx (xx.x%)	xxx (xx.x%)
Week 168	xxx (xx.x%)	xxx (xx.x%)
Week 180	xxx (xx.x%)	xxx (xx.x%)
Week 192	xxx (xx.x%)	xxx (xx.x%)

Repeat for other RA augmented therapy as reported in CRFs

Abbreviations: COL, Control to Open Label; cs/b/tsDMARD, conventional synthetic, biologic or targeted synthetic disease-modifying anti-rheumatic drug; TOL, Treament to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL)
[4] Percentage calculated based on the start date noted on the Concomitant Medication log

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.2.20
Implant Performance

Variable	TOL [1]	COL [2]	Overall
Status of study implant at study exit [3]	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with active implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with suspended implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects with explanted implant	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unknown	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Abbreviations: COL, Control to Open Label; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL, Overall)

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Table 14.8.3.1
Adverse Events

Variable	TOL [1] (N=xxx) Events n (%)	COL [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)
Any AE [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Not Related [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Related [4][5]			
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Indeterminate [4]			
Implant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE resulting in discontinuation [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE by maximum severity [4]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure related AE by maximum severity [4][5]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Variable	TOL [1] (N=xxx) Events n (%)	COL [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)
Implant Device AE by maximum severity [4][5]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation related AE by maximum severity [4][5]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Energizer related AE by maximum severity [4][5]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure related AE by maximum severity [4][5]			
Mild	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Moderate	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Severe	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
SAE [4][5]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Procedure SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Implant Device SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Energixer SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Explant Procedure SAE	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; COL, Control to Open Label; SAE, serious adverse event; TOL, Treatment to Open Label
Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE

Variable	TOL [1] (N=xxx) Events n (%)	COL [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects.
[4] Percentage calculated based on each analysis population (i.e., TOL, CL, Safety).
[5] AEs judged to be "Definitely related" or "Probably related" are reported as "Related".

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.3.2
Adverse Events by SOC and Maximum Severity: All Events

SOC Preferred Term	TOL [1] (N=xxx)				COL [2] (N=xxx)				Safety Population [3] (N=xxx)			
	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)
Any AE [4]	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 (xx%)
SOC 1 [4]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
SOC 2 [4]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)

Continue …

Abbreviations: AE, adverse event; COL, Control to Open Label; SOC, system organ class; TOL, Treatment to Open Label

Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE.

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects.
[4] Percentage calculated based on each analysis population (i.e., TOL, CL, Safety).

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.3.3
Implant Procedure-Related AEs by SOC and Maximum Severity: All Events

SOC Preferred Term	TOL [1] (N=xxx)				COL [2] (N=xxx)				Safety Population [3] (N=xxx)			
	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)	Mild Events n (%)	Moderate Events n (%)	Severe Events n (%)	Total Events n (%)
Any AE [4][5]	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 (xx%)
SOC 1 [4][5]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)
SOC 2 [4][5]	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 (xx%)
Preferred Term 1	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 (xx%)
Preferred Term 2	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 (xx%)
Preferred Term 3	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 (xx%)
Preferred Term 4	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 (xx%)

Continue …

Abbreviations: AE, adverse event; COL, Control to Open Label, SOC, system organ class; TOL, Treatment to Open Label

Note: AEs coded using the MedDRA dictionary Version 21.0 or later. Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subjects experiencing AEs of more than one severity are summarized according to the maximum severity experienced over all episodes of an AE.

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects.
[4] Percentage calculated based on each analysis population (i.e., TOL, CL, Safety).
[5] AEs judged to be "Definitely related" or "Probably related" are reported as "Related".

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.3.4
Implant Device-Related AEs by SOC and Maximum Severity: All Events

Repeat Table 14.8.3.3 for implant device-related adverse events

Table 14.8.3.5
Stimulation-Related AEs by SOC and Maximum Severity: All Events

Repeat Table 14.8.3.3 for stimulation-related adverse events

Table 14.8.3.6
Energizer-Related AEs by SOC and Maximum Severity: All Events

Repeat Table 14.8.3.3 for Energizer-related adverse events

Table 14.8.3.7
Explant Procedure-Related Adverse Events by SOC and Maximum Severity: All Events

Repeat Table 14.8.3.3 for explant procedure-related adverse events

Table 14.8.3.8
Device Deficiency

Variable	TOL [1] (N=xxx) Events n (%)	COL [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)
Any study device deficiency [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Relationship of study device deficiency [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
MicroRegulator (Implant)	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
POD	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Energizer	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Stimulation	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Prescription Pad	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
IFU/Labeling	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Study device deficiency associated with AE [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Study device deficiency associated with SAE [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; COL, Control to Open Label; POD, Positioning Orientation Device; SAE, serious adverse event; SOC, system organ class; TOL, Treatment to Open Label

Note: Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once. Subject experiencing several episodes of the same type of study device deficiency is counted once.

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects.
[4] Percentage calculated based on each analysis population (i.e., TOL, CL, Safety).

Reference: Listing 16.x.x.x
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}

Table 14.8.3.9
Protocol Deviations

Variable	OL PTE [1] (N=xxx) Events n (%)	CO PTE [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)
Any protocol deviation [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Minor protocol deviations [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Improper documentation of consent	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment not done	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment completed out of window	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
AE not reported within required schedule	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Received medication not allowed per protocol	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Subject or study staff unblinded	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Other, specify	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations due to COVID-19 [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment not done	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment completed out of window	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Visit or assessment completed not per protocol	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations associated with AE [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)
Protocol deviations associated with SAE [4]	xx xx (xx.x%)	xx xx (xx.x%)	xx xx (xx.x%)

Abbreviations: AE, adverse event; COL, Control to Open Label; SAE, serious adverse event; TOL, Treatment to Open Label
Note: Given in the table are subject counts and percentages. At each level of summation, subjects are counted only once.

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Safety population comprises all enrolled subjects.
[4] Percentage calculated based on each analysis population (i.e., TOL, CL, Safety).

Reference: Listing 16.x.x.x

Variable	OL PTE [1] (N=xxx) Events n (%)	CO PTE [2] (N=xxx) Events n (%)	Safety Population [3] (N=xxx) Events n (%)
SOURCE: xxxxx SAS 9.4 {program location} {run date/time}}			

Appendix C: Listing Mockups

Listing 16.8.2.1
Subject Disposition

Analysis Population	Subject ID	Consent Date	Implant Procedure Date	Day 0 Date	Week 12 Date	Subject Status	Date of Exit	Reason for Withdrawal	Implant Status at Study Exit
TOL	xx-xxxx	DD-MMM-YYYY	DD-MMM-YYYY	DD-MMM-YYYY					
COL	xx-xxxx	DD-MMM-YYYY	DD-MMM-YYYY	DD-MMM-YYYY					

Programming notes:

This listing will include all subjects from Control to Open Label (COL) and Treatment to Open Label (TOL) populations for whom follow-up data are available.

Subject Status: Withdrawn, Completed Study.

Reason for withdrawal: Subject decision to withdraw consent, Investigator decision or medical judgement, Lost to follow-up, Device malfunction, Adverse event, Subject no longer eligible, Death, Study terminated, Sponsor or IRB decision, Other

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.2
Protocol Deviations

Analysis Population	Subject ID	Deviation ID	Visit	Deviation Date	Classification	Category	Reason	Associated with AE?	Associated with SAE?	Reported to IRB?	Description
	xx-xxxx										
	xx-xxxx										

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.3
Analysis Populations

Subject ID	Population	
	TOL [1]	COL [2]
xx-xxxx	Yes	No
xx-xxxx	No	Yes
xx-xxxx	No	Yes

Abbreviations: COL, Control to Open Label; ITT, intent to treat; TOL, Treatment to Open Label

[1] Treatment to Open Label (TOL): The TOL population comprises treatment subjects from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.

[2] Control to Open Label (COL): The COL population comprises control subjects from ITT population who received non-active (sham) stimulation through Week 12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.4
Concomitant Medication

Analysis Population	Subject ID	ATC level Preferred Term/ Medication	Start Date	Start Study Day	Stop Date	Stop Study Day	Primary Indication	Dosage (Unit)	Route	Frequency
OL PTE	xx-xxxx									
CO PTE	xx-xxxx									

Programming notes:

- This listing will include all subjects from OL PTE and CO PTE populations for whom follow-up data are available.
- If Ongoing is checked "Yes" list "Ongoing" under stop date column
- Concatenate dose and unit for listing, if other unit exists then list it for units
- Route, if Other Route is not blank, list it under "Route" column
- Frequency, if Other Frequency is not blank, list it under 'Frequency" Column

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.5
Subjects Receiving Augmented Treatment After Week 12

Subject ID	CDAI at baseline	CDAI prior to start of augmented therapy	Type of augmented therapy	Start date / Stop date	Therapy started prior to Week 12? (Y/N)	Therapy start relative to Day 0 (days)
xx-xxxx	Baseline: xx.x	Day 0: xx.x				

Listing 16.8.2.6.1
Explant Procedure

Population Analysis	Subject ID	Explant Procedure Date	MicroRegulator Serial#	MicroRegulator Explanted?	Post-Op Clearance Date	Any AEs?
TOL						
	xx-xxxx					
COL						
	xx-xxxx					

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.6.2
Stimulation Prescription
(Part 1)

Analysis Population	Subject ID	Visit	Strength (uA)	Duration	Frequency	Schedule	Dose Changed at this Visit?	Dose Change Reason
TOL								
	xx-xxxx							
	xx-xxxx							
COL								
	xx-xxxx							
	xx-xxxx							

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.6.2
Stimulation Prescription
(Part 2)

Analysis Population	Subject ID	Energizer Battery Charge	Energizer App Firmware	Energizer Bluetooth Firmware	Implant App Firmware	Implant Impedance	MicroRegulator Suspended?/Reason
TOL							
	xx-xxxx						
	xx-xxxx						
COL							
	xx-xxxx						
	xx-xxxx						

Listing 16.8.2.7.1
RA Disease Activity Assessments

Analysis Population	Subject ID	Visit	SJC28 Score	TJC28 Score	HAQ-DI Score	Subject's Pain Score	SGA Score	EGA Score	hsCRP (mg/mL)
TOL									
	xx-xxxx								
		Screening	xx	xx	xxx	xxx	xx	xxx	xx
		Day 0							
		Week 12							
		Week 24							
		Week 36							
		Week 48							
		Week 60							
		Week 72							
		Week 84							
		Week 96							
		Week 108							
		Week 120							
		Week 132							
		Week 144							
		Week 156							
		Week 168							
		Week 180							
		Week 192							
COL									

Listing 16.8.2.7.2
ACR20 Response from Baseline

				Reduced by at least 20%?						
Analysis Population	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168	2							
		Week 180								

				Reduced by at least 20%?						
Analysis Population	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
		Week 192								

Note: Response defined by at least 70% reduction from baseline (i.e., on the day of informed consent for TOL and Week 12 for COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location}{run date/time}

Listing 16.8.2.7.2.1
ACR20 Response from Initiation of Stimulation

				Reduced by at least 20%?						
Analysis Population	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								

				Reduced by at least 20%?						
Analysis Population	Subject ID	Visit	ACR20 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP

Note: Response defined by at least 20% reduction from initiation of stimulation (i.e., Day 0 for subjects in TOL, and Week 12 for subjects in COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

Note to programmer:
Subjects from both TOL and COL populations are listed here.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.3
ACR50 Response from Baseline

				Reduced by at least 50%?						
Analysis Population	Subject ID	Visit	ACR50 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								

				Reduced by at least 50%?						
Analysis Population	Subject ID	Visit	ACR50 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
		Week 180								
		Week 192								

Note: Response defined by at least 70% reduction from baseline (i.e., on the day of informed consent for TOL and Week 12 for COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.3.1
ACR50 Response from Initiation of Stimulation

				Reduced by at least 50%?						
Analysis Population	Subject ID	Visit	ACR50 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								

				Reduced by at least 50%?						
Analysis Population	Subject ID	Visit	ACR50 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP

Note: Response defined by at least 50% reduction from initiation of stimulation (i.e., Day 0 for subjects in TOL, and Week 12 for subjects in COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.4
ACR70 Response from Baseline

				Reduced by at least 70%?						
Analysis Population	Subject ID	Visit	ACR70 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								

				Reduced by at least 70%?						
Analysis Population	Subject ID	Visit	ACR70 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
		Week 180								
		Week 192								

Note: Response defined by at least 70% reduction from baseline (i.e., on the day of informed consent for TOL and Week 12 for COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.4.1
ACR70 Response from Initiation of Stimulation

				Reduced by at least 70%?						
Analysis Population	Subject ID	Visit	ACR70 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP
TOL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								
COL										
	xx-xxxx	Week 24	N	N	N	N	N	N	N	N
		Week 36	N	N	N	N	N	N	N	N
		Week 48	Y	N	N	N	N	N	N	N
		Week 60	Y	Y	Y	N	Y	Y	N	Y
		Week 72	N	N	N	N	N	N	N	N
		Week 84	Y	N	N	N	N	N	N	N
		Week 96								
		Week 108								
		Week 120								
		Week 132								
		Week 144								
		Week 156								
		Week 168								
		Week 180								
		Week 192								

				Reduced by at least 70%?						
Analysis Population	Subject ID	Visit	ACR70 Response	SJC28	TJC28	HAQ-DI	Subject's Pain	SGA	EGA	hsCRP

Note: Response defined by at least 70% reduction from initiation of stimulation (i.e., Day 0 for subjects in TOL, and Week 12 for subjects in COL) in TJC28 and SJC28 and 3 our 5 outcomes, according to ACR definition.

Note to programmer:
Subjects from both TOL and COL populations are listed here.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.5
CDAI

Population Analysis	Subject ID	Visit	CDAI Score	LDA (>2.8 to ≤ 10)	Remission (0 to ≤ 2.8)	MCID from Baseline	MCID from Initiation of Stimulation
TOL							
	xx-xxxx	Baseline	xx.x	N	N	–	–
		Day 0	xx.x	N	N	N	–
		Week 12	xx.x	N	N	N	N
		Week 24		Y	N	Y	Y
		Week 36		Y	Y	Y	Y
		Week 48					
		Week 60					
		Week 72					
		Week 84					
		Week 96					
		Week 108					
		Week 120					
		Week 132					
		Week 144					
		Week 156					
		Week 168					
		Week 180					
		Week 192					
COL							
	xx-xxxx	Week 12	xx.x	N	N	–	–
		Week 24		Y	N	Y	Y
		Week 36		Y	Y	Y	Y
		Week 48					
		Week 60					
		Week 72					
		Week 84					
		Week 96					
		Week 108					
		Week 120					
		Week 132					
		Week 144					
		Week 156					

Population Analysis	Subject ID	Visit	CDAI Score	LDA (>2.8 to ≤ 10)	Remission (0 to ≤ 2.8)	MCID from Baseline	MCID from Initiation of Stimulation
		Week 168					
		Week 180					
		Week 192					

Note: The MCID varies depending on RA disease activity at baseline (i.e., on the day of informed consent for TOL and at Week 12 for COL) or initiation of stimulation (TOL, COL): -12 for high activity (CDAI > 22), -6 for moderate activity (>10 to ≤ 22), or 1 if low disease activity (>2.8 to ≤ 10).

Note to programmer: Baseline on the day of informed consent for TOL and at Week 12 for COL.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.6
DAS28-CRP

Population Analysis	Subject ID	Visit	DAS28-CRP Score	LDA (0.6 to < 3.2)	Remission (0 to < 2.6)	MCID from Baseline (-1.2)	MCID from Initiation of Stimulation (-1.2)	DAS28-CRP Good/Moderate EULAR Response
TOL								
	xx-xxxx	Baseline	xx	N	N	--	–	--
		Day 0	xx	N	N	N	–	N
		Week 12	xx	Y	N	Y	Y	Moderate
		Week 24	xx	Y	Y	Y	Y	Good
		Week 36						
		Week 48						
		Week 60						
		Week 72						
		Week 84						
		Week 96						
		Week 108						
		Week 120						
		Week 132						
		Week 144						
		Week 156						
		Week 168						
		Week 180						
		Week 192						
COL								
	xx-xxxx	Week 12	xx	N	N	--	–	--
		Week 24	xx	N	N	N	Y	N
		Week 36	xx	Y	N	Y	Y	Moderate
		Week 48	xx	Y	Y	Y	Y	Good
		Week 60						
		Week 72						
		Week 84						
		Week 96						
		Week 108						
		Week 120						
		Week 132						
		Week 144						

Week 156
Week 168
Week 180
Week 192

Note to programmer: Baseline on the day of informed consent for TOL and at Week 12 for COL.

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.7
HAQ-DI

Population Analysis	Subject ID	Visit	HAQ-DI Score	MCID from Baseline (-0.22)	MCID from Initiation of Stimulation
TOL					
	xx-xxxx	Baseline	xx	--	--
		Day 0	xx	N	--
		Week 12	xx	N	N
		Week 24	xx	Y	Y
		Week 36	xx	Y	Y
		Week 48			
		Week 60			
		Week 72			
		Week 84			
		Week 96			
		Week 108			
		Week 120			
		Week 132			
		Week 144			
		Week 156			
		Week 168			
		Week 180			
		Week 192			
COL					
	xx-xxxx	Week 12	xx	--	--
		Week 24	xx	N	N
		Week 36	xx	Y	Y
		Week 48	xx	Y	Y
		Week 60			
		Week 72			
		Week 84			
		Week 96			
		Week 108			
		Week 120			
		Week 132			
		Week 144			
		Week 156			

Population Analysis	Subject ID	Visit	HAQ-DI Score	MCID from Baseline (-0.22)	MCID from Initiation of Stimulation
		Week 168			
		Week 180			
		Week 192			

Note to programmer: Baseline on the day of informed consent for TOL and at Week 12 for COL

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.8
RAMRIS

Population Analysis	Subject ID	Visit	Synovitis Score	Osteitis score	Bone Erosion score	Progression? (Bone Erosion Increase > 0.5)	CARLOS
TOL	xx-xxxx	Baseline (Screening)	xx	xx	xx	–	xx
		Week 24				–	
		% Change from baseline				N	
COL	xx-xxxx	Baseline (Week 12)					
		Week 24					
		Change from baseline					

Note to programmer: Baseline during Screening for TOL and at Week 12 for COL

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.9
EQ-5D-5L

Population Analysis	Subject ID	Visit	Mobility	Self-Care	Usual Activities	Pain/Discomfort	Anxiety/Depression	EQ-VAS	Index value
TOL									
	xx-xxxx	Week 24 Week 48 Week 96 Week 144	x	x	x	x	x	xxx	xx
COL									
	xx-xxxx	Week 24 Week 48 Week 96 Week 144 Week 192	x	x	x	x	x	xxx	xx

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.10
SF-36

Population Analysis	Subject ID	Visit	PCS score	MCS score
TOL				
	xx-xxxx	Week 24		
		Week 48		
		Week 96		
		Week 144		
COL				
	xx-xxxx	Week 24		
		Week 48		
		Week 96		
		Week 144		
		Week 192		

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.11
Subject Satisfaction

Population Analysis	Subject ID	Visit	How satisfied are you with the SetPoint System for treatment of your RA	Would you recommend it to a family member or a friend?	Comment
TOL					
	xx-xxxx	Week 24	Very satisfied	Yes	
	xx-xxxx	Week 24	Satisfied	Yes	
	xx-xxxx	Week 24	Neither satisfied nor dissatisfied	No	
	xx-xxxx	Week 24	Somewhat dissatisfied	No	
	xx-xxxx	Week 24	Very dissatisfied	No	
COL					
	xx-xxxx	Week 24	Very satisfied	Yes	
	xx-xxxx	Week 24	Satisfied	Yes	
	xx-xxxx	Week 24	Neither satisfied nor dissatisfied	No	
	xx-xxxx	Week 24	Somewhat dissatisfied	No	
	xx-xxxx	Week 24	Very dissatisfied	No	

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.7.12
Inflammatory Biomarkers

Population Analysis	Subject ID	Visit	IL-6 (pg/mL)	IL-6 % Change	SAA (µg/mL)	SAA % Change	MMP-3 (pg/mL)	MMP-3 % Change
TOL								
	xx-xxxx	Baseline		–		--		--
		Day 0						
		Week 12						
		Week 24						
		Week 36						
		Week 48						
		Week 60						
		Week 72						
		Week 84						
		Week 96						
		Week 108						
		Week 120						
		Week 132						
		Week 144						
		Week 156						
		Week 168						
		Week 180						
		Week 192						
COL								
	xx-xxxx	Week 12		–		--		--
		Week 24						
		Week 36						
		Week 48						
		Week 60						
		Week 72						
		Week 84						
		Week 96						
		Week 108						
		Week 120						
		Week 132						
		Week 144						

Week 156
Week 168
Week 180
Week 192

Note to programmer: Percent change from baseline (i.e., Screening for TOL and at Week 12 for COL).

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.8
Adverse Events

Analysis Population	Subject ID	System Organ Class/ Preferred Term/ Adverse Event Verbatim	Onset Date (Day)	Resolution Date (Day)	Severity	SAE?	Relationship	Treatment/ outcome
TOL	xx-xxxx	xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/ xxxxxx/	DD-MMM-YYYY (xx)	DD-MMM-YYYY (xx)				xxxxxx/ xxxxxx
COL	xx-xxxx	None						

Note: If a Subject has no AEs then "None" will be displayed. Adverse Events are coded in MedDRA V21.0 or later.

Note to programmer: If Ongoing is checked then list "Continuing" in the place for "Resolution Date (Day)".

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}

Listing 16.8.2.9
Device Deficiencies

Analysis Population	Subject ID	Deficiency ID	Deficiency Date	Deficiency Related To	Associated with AE?	Associated with SAE?	Description
TOL							
	xx-xxxx						
COL							
	xx-xxxx						

SOURCE: xxxxx SAS 9.4 {program location} {run date/time}