Non-Interventional Study Protocol
B7451089

Prospective, single-arm, multicenter, observational non-interventional study (NIS) in Germany of patient characteristics, usage and effectiveness of abrocitinib in patients with moderate to severe atopic dermatitis (AD)

Statistical Analysis Plan
(SAP)

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1 INTRODUCTION

AD is a common inflammatory skin disease characterized by pruritus, eczematous lesions and its chronically relapsing course. For European countries, a prevalence of 4.4% was estimated among adults based on survey data from 2016 [1]. In Germany, approximately 13% of children and adolescents aged 0-17 years are at least temporarily affected by AD [2]. Skin manifestations typically start in childhood and can persist into adulthood [3].

Clinical signs of AD are pruritus and eczematous lesions with unpredictable periods of acute worsening (exacerbation of signs and symptoms/exacerbations) alternating with periods of relative calm after treatment. Chronic lesions are characterized by lichenification, nodulation and excoriation, and patients usually have a dry, flaky skin.

Although great strides have been made in understanding the causes, the complex pathophysiology of AD is still not completely understood. It has been established that the pathophysiology of AD includes a defective skin barrier function, allergic responses, defective antimicrobial immune defense, and a genetic predisposition. The predominant symptom of AD is pruritus, and the resulting scratching typically sets off an amplification cycle of atopic skin inflammation with an immense impact on the patients´ quality of life, including physical and psychosocial effects on both patients and families [4]. The health-related impact on quality of life (QoL) correlates with disease severity and exceeds that seen in patients affected with diseases like asthma, epilepsy, and diabetes. Comorbidities include sleep deprivation from pruritus (more than 60% of AD cases), pain, anxiety, depression, suicidal ideation, obesity, food allergies, asthma, and allergic rhinitis/rhino conjunctivitis, which can be debilitating and negatively impact all areas of personal, academic, professional, and daily life for the patient and family members [4,5]. Therefore, one of the most important treatment goals should be a reduction of pruritus and that patients can report freedom from itching.

Current Standard of Care

AD management aims to improve symptoms and establish long-term disease control by avoidance of individual trigger factors, skin barrier restoration through moisturizer use, and a step-up/step-down approach aimed at reducing inflammation [6]. The choice of anti-inflammatory-therapy is largely based on AD severity/activity; mild AD can usually be controlled with topical treatments; more severe disease may require phototherapy and/or systemic immunomodulatory therapy [7]. Systemic treatment of AD is usually reserved for patients with refractory and severe disease where topical treatments of AD are not effective or have not been well tolerated. Currently only a limited number of treatments are available especially for patients with severe AD: Systemic therapy options, such as oral corticosteroids, immunomodulators such as Ciclosporin (Cyclosporin A) are associated with potentially severe adverse effects and require careful monitoring. For these reasons, the use of these agents is limited to short courses or intermittent therapy. Further, none offers a cure; therefore, the main aims of existing treatments are to reduce the occurrence of acute flares, to increase the time between

relapses, and to reduce pruritus and the resulting sleep disturbance [7-9]. Other systemic agents to treat AD are under clinical development or recently approved.

In Germany dupilumab, an injectable monoclonal antibody directed against interleukin-4 receptor alpha, was approved in 2017 and offers a novel mechanism of action for the treatment of patients (>12 years) with moderate to severe AD and children (>6 years) for the treatment of severe AD. Dupilumab inhibits signaling of interleukin (IL)-4 and IL-13, and by doing so alters type 2 helper T (Th2) cell-mediated immune responses and improves epidermal barrier abnormalities in AD. While efficacy results from clinical studies of dupilumab are compelling [10], a large proportion of subjects fail to achieve a favorable response of Investigator's Global Assessment (IGA) 0-1/Eczema Area and Severity Index (EASI-75) and continue to experience the burden of moderate to severe AD. Additionally, a slow onset of action (2 to 4 weeks), and an incomplete relief of pruritus highlights the need for faster-acting therapies that work in a larger percentage of patients, especially on pruritic symptoms. In addition, treatment with dupilumab has the risk of injection site reactions, allergic reactions, eye and eyelid inflammations and cold sores [11]. Furthermore, dupilumab is delivered via subcutaneous injection, which may not be a method of administration tolerated well by all patients.

In June 2021, the second injectable monoclonal antibody, tralokinumab received drug approval by the European Medicines Agency (EMA) for the treatment of adult patients with moderate to severe atopic dermatitis who are candidates for systemic therapy. Tralokinumab neutralizes IL-13, a cytokine which is supposed to play a key role in AD [12]. The effectiveness of tralokinumab monotherapy has been shown in the ECZTRA 1 and ECZTRA 2 trials [13]. Besides very commonly reported side effects like upper respiratory tract infections and commonly reported side effects like eye redness and itching, eye infections, and injection side reactions, tralokinumab very rarely can cause serious side effects including hypersensitivity reactions such as anaphylaxis [14].

Baricitinib, a JAK1/2 inhibitor, has been approved in 2020 as first small molecule for adult patients with moderate to severe AD who are eligible for systemic therapy. Baricitinib is taken orally as a tablet. According to the applicable summary of product characteristics of baricitinib, laboratory monitoring of lipid parameters, neutrophil count, lymphocyte count, hemoglobin, and liver transaminases should be performed while taking baricitinib. The use of baricitinib is associated with an increased risk of infections such as upper respiratory tract infections [15]

Most recently (in July 2021), upadacitinib a JAK1 inhibitor as second small molecule has been approved by the EMA for the treatment of adults and adolescents (≥12 years) with moderate to severe atopic dermatitis. Like baricitinib, upadacitinib is also taken orally as a tablet. According to the applicable Summary of Product Characteristics (SmPC) monitoring of neutrophil and lymphocyte count, hemoglobin, liver transaminases, and lipid parameters is strictly recommended. Also, upadacitinib use is associated with an increased risk of infections. The most frequent serious infections reported with upadacitinib included pneumonia and cellulitis [16].

However, there is still an unmet medical need for a conveniently administered therapy with an acceptable safety profile, for continuous and intermittent use, which is effective for moderate to severe AD and has a rapid onset of action including for the relief of pruritus.

Abrocitinib: Mechanism of Action (MoA)

Abrocitinib (PF-04965842) is an orally bioavailable small molecule being developed as an oral treatment for patients with moderate to severe AD, therefore it provides a more convenient route of administration compared with the subcutaneous injection required for dupilumab and does not have the potential risk of injection site reactions. Unlike dupilumab, abrocitinib is a small molecule and there is no anticipated immunogenicity to abrocitinib, and so it is unlikely to generate antidrug antibodies and may be used intermittently.

Abrocitinib selectively inhibits JAK-1 by blocking the adenosine triphosphate (ATP) binding site. It has a high degree of selectivity against other kinases in the human genome: 28-fold selectivity over JAK-2, >340-fold over JAK-3 and 43-fold over tyrosine kinase 2 (TYK2) as well as a good selectivity profile over the broader range of human kinases. A variety of pro-inflammatory cytokines such as IL-4, IL-5, IL-13, IL-31 and IFN-γ, have been suggested to be involved in the pathogenesis of AD. Many of these pathogenic cytokines use JAK-1 for signaling. This suggests that selective JAK-1 inhibitors that modulate the activity of these cytokines represent a compelling approach to the treatment of inflammatory skin diseases such as AD [17]. Broader inhibition of cytokines, including those important in the pathogenesis of AD, may result in an increased proportion of responders, with an acceptable safety profile.

The first Phase 3 studies, B7451012 and B7451013, that evaluated 100 and 200 mg once daily (QD) abrocitinib in participants with moderate to severe AD, which were completed in 2019, reported statistically significant improvement in efficacy endpoints in both treatment groups compared to the placebo group, with an acceptable safety profile [18,19].

Summary of Study Rationale

Currently, there is a lack of real-world data regarding the effectiveness of the new systemic treatment class of JAK inhibitors in AD in daily clinical practice in Germany. Thus, this non-interventional study was designed to gather information about non-selected patients who have been chosen to start treatment with abrocitinib in dermatological practices in Germany.

In order to gain valuable and solid insights into current and upcoming real-world treatment patterns starting with a systemic abrocitinib therapy, all subsequent therapy sequences with reasons for the respective therapy decisions will be systematically documented. Specific information on the patient´s medical and clinical history, the routine clinical management including the reasons for starting treatment, management of treatment initiation, prescribed concomitant medication, its dosage, and actual use by the

treated patient will be recorded. In order to understand not only the treatment management and reasons for starting treatment with abrocitinib, but also the reasons for ending therapy with abrocitinib, all patients will be followed up for the full individual observation period of 12 months after first abrocitinib prescription after inclusion in this observational study regardless of whether they are constantly treated with abrocitinib.

Taking into account the more diverse patient population in the real-world setting, this non-interventional study will further provide additional short-and long-term real-world evidence for the effectiveness of abrocitinib in patients of medical interest and need, who may have been underrepresented in the controlled settings of clinical trials and evaluate patient-relevant endpoints including measurements of patient-reported outcomes, such as quality of life, depression, pruritus, and sleep quality.

Patient preference and satisfaction of a therapy strongly affects adherence to a prescribed medication, ultimately affecting treatment outcome and efficacy. A factor known to have an impact on patient satisfaction with a prescribed treatment is the route of administration. Here, several studies point to a preference for oral therapies. Thus, this non-interventional study will document patient's expectations and satisfaction with regards to the treatment.

Based on the collected patient characteristics (i.e., severity/duration of disease, pretreatment, comorbidities) and the heterogeneity of patient profiles encountered in a real-world setting, potential predictors of response and prognostic factors for an optimal treatment can be identified and on some of them shall be further elaborated. Hand eczema with its atopic subtype [20] already has a strong association with atopic dermatitis. [20] For instance, with atopic dermatitis and hand eczema, both, the skin barrier dysfunction associated with filaggrin mutations, is relevant [21,22]. The treatment of hand eczema is quite challenging, but anti-inflammatory treatment is important; [20,23] including JAK inhibition as an interesting new therapy approach [23,24]. The association of AD and asthma is well established [25]. It is now recognized that type 2 cytokines, like IL-4, IL-5 and IL-13, play an important pathophysiological role. [26] Successfully conducted clinical trials with dupilumab in patients with uncontrolled persistent asthma [26] and moderate-to-severe uncontrolled asthma [27] resulted in the end with a market authorization of dupilumab as add-on maintenance treatment for severe asthma with type 2 inflammation in the European Union [11]. Also allergic rhinitis and polyposis nasi, as atopic morbidities, are driven by type 2 inflammation [28], resulting in market authorization for dupilumab in the European Union for chronic rhinosinusitis with nasal polyposis [11]. Also in alopecia areata, clinical trials with JAK inhibition were conducted successfully [29,30] with baricitinib gaining market authorization in the European Union [31]. Prurigo nodularis and AD share JAK inhibition as a same treatment target (binding of IL-31 to its respective receptor [32,33] mediated through a JAK1 and JAK2 signaling pathway [34]) showing efficacy against pruritus [33]. Consequently, the impact of adequately treated AD with abrocitinib on comorbidities of interest, such as (allergic) asthma, (allergic) rhinitis, polyposis nasi, chronic hand eczema, as well as other commonly associated

comborbidities, like prurigo nodularis [32,35] and alopecia areata, [36,37] shall be assessed.
Above shown information will help to draw inferences and optimize future therapy with abrocitinib and its clinical management.

1.1 STUDY DESIGN

This prospective, single-arm, multi-center, observational non-interventional study in Germany does not interfere with the current routine practice of the treating physician. All treatment decisions, types and timing of disease monitoring, diagnostic or other medicinal procedures are at the discretion of the treating physician and patients and are not influenced or affected by the participation in this non-interventional study.

All assessments described in this protocol are performed as part of normal clinical practice or standard practice guidelines for the patient population and healthcare provider specialty in the countries where this non-interventional study is being conducted. There will be no additional diagnostic or monitoring procedures that are outside the routine clinical practice.

This is a 60-month, prospective, non-interventional, multicenter study to evaluate the effectiveness, usage and patient characteristics of real-world use of abrocitinib in patients with moderate to severe AD in a real-world setting.

Eligible patients will be followed up for 12 months from the date of enrollment. Patients who are switched from abrocitinib therapy to other therapies continue to be observed. Patient documentation is expected quarterly as per standard clinical practice.

Strength of this non-interventional study is the observation of drug prescription and follow-up visits in a daily medical care setting. Therapeutic strategies, patient selection and frequency of patient follow-up are decided by the treating physician.

The recommended schedule of activities table provides an overview of the visits that may be documented. As this is a non-interventional study none of these visits are mandatory and every visit should be scheduled according to clinical practice. According to clinical practice the HCP may schedule additional visits to those listed on the schedule of activities, in order to conduct evaluations or assessments required to protect the well-being of the patient.

Table 1. Recommended Schedule of Activities

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**
Informed consent	X					
Inclusion/exclusion criteria	X					
Demographic data of patient (age, sex, weight, height, ethnicity, race, smoker/non-smoker, education, occupation, alcohol consumption, insurance type)	X					
Family history of atopic diseases	X					
Clinical history (Herpes simplex, eczema herpeticum, herpes zoster)	X					
Renal and/or liver impairment	X					
Vaccination status (Herpes zoster, Covid-19, Influenza, Varicella)	X					X
Age at initial diagnosis of AD	X					

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
Previous treatments for diagnosed AD	X					
Current comorbidities	X					
If positive anamnesis at baseline exists: Improvement of asthma symptoms from baseline						X
If positive anamnesis at baseline exists: Improvement of allergic rhinitis symptoms from baseline						X
If positive anamnesis at baseline exists: Improvement of polyposis nasi symptoms from baseline						X
If positive anamnesis at baseline exists: Improvement of alopecia areata from baseline						X
If positive anamnesis at baseline exists: Improvement of prurigo nodularis from baseline						X
If positive anamnesis at baseline exists:						X

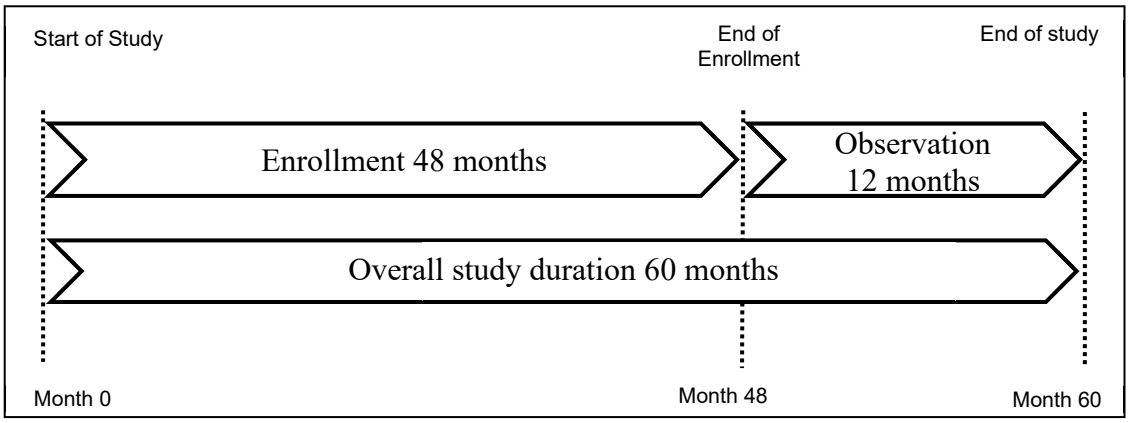
Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
Improvement of hand eczema from baseline						
Number of flares during the last 12 months (first visit) and since the last visit (regardless of abrocitinib treatment status*)	X	X	X	X	X	X
Number of hospitalizations due to AD during the last 12 months (first visit) and since the last visit (regardless of abrocitinib treatment status*)	X	X	X	X	X	X
Number of absent days at work/study due to AD one year before start of treatment with abrocitinib (first visit) and since the last visit (regardless of abrocitinib treatment status*)	X	X	X	X	X	X
Reasons for start of therapy with abrocitinib	X					
Reasons for discontinuation of therapy with abrocitinib		X	X	X	X	X

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
Compliance with abrocitinib treatment		X	X	X	X	X
Dosage of abrocitinib used	X	X	X	X	X	X
Reasons for prescribed dosage	X	X	X	X	X	X
Type and results of laboratory check controls	X	X	X	X	X	X
Adverse events		X	X	X	X	X
Concomitant treatment AD specific (type and dosage)	X	X	X	X	X	X
Number of days with topical- treatment use (TCS, TCI) & days with emollients use three months before start of treatment with abrocitinib (first visit) and since the last visit (regardless of abrocitinib treatment status*)	X	X	X	X	X	X
Concomitant (non-AD) treatment	X					
SCORAD	X	X	X	X	X	X
EASI	X	X	X	X	X	X

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
IGA	X	X	X	X	X	X
Pruritus-NRS	X	X	X	X	X	X
PP-NRS	X	X	X	X	X	X
DLQI	X	X	X	X	X	X
POEM	X	X	X	X	X	X
MOS	X	X	X	X	X	X
PBI	X	X	X	X	X	X
EQ-5D-5L	X	X	X	X	X	X
HADS	X	X	X	X	X	X

* This includes patients who discontinued treatment with abrocitinib.

Figure 1. Timelines



The planned observation period of each patient is 12 months. In this time period up to 6 visits will be documented.

Figure 2. Study Period

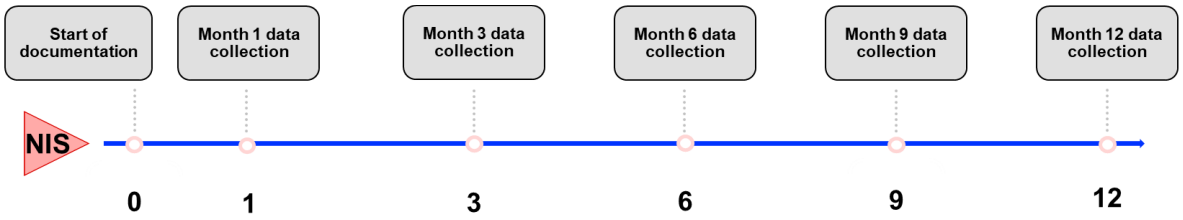


Table 2. Definition of time windows for study visits

In order to collect comparable study data, Visits 1 to 3 occurring ±14 days and Visits 4 to 6 occurring ±28 days of the scheduled visit date will be used for data analysis (interim analysis).

Visit Label	Target Day	Definition [Day window]
Enrolment	1	1
Month 1	30	16 to 44
Month 3	91	77 to 105
Month 6	182	154 to 210
Month 9	273	245 to 301
Month 12	365	337 to 393

Visits that do not meet the defined windows as displayed in the table above will also be included in the final analysis and clinical study report. Therefore, all visits will be included using the visit time slots shown below. If more than one visit appears in a 3-month window, only the visit closest to the target day will be respected.

Amended definition:

Visit designation	Target Day	Definition [Day window]
Enrolment	1	1
Month 1	30	2 to 44
Month 3	91	45 to 105
Month 6	182	106 to 210
Month 9	273	211 to 301
Month 12	365	302 to 393

However, for analysis of safety parameters, all AEs/SAEs documented within the applicable reporting period will be analyzed.

- *For the lab values, if the calculated study day for the labelled baseline visit is not study Day 1, but falls within 40 days before the start of the study dosing, then that data should be used for the baseline instead of leaving baseline missing.*
- *For the other values, if the calculated study day for the labelled baseline visit is not study Day 1, but falls before the start of the study dosing, then that data should be used for the baseline instead of leaving baseline missing.*
- *If baseline is missing there will be no imputation and although the subject's data will be included in summary data it will not be included in any change from baseline analyses.*

If two or more routine visits fall into the same window, keep the one closest to the Target Day. If two routine visits are equal distance from the Target Day in absolute value, the later visit should be used.

1.2 STUDY POPULATION

In total, this non-interventional study aims to enroll at least 750 patients patients at approximately 80 study sites across Germany. The planned enrollment period is 48 months. With a planned observation duration of 12 months per patient, the entire study would last for 60 months. The non-interventional study started in April 2022 and will end in May 2027.

1.3 STUDY OBJECTIVES

The objectives of this non-interventional study are to examine patient characteristics, usage and effectiveness of abrocitinib in adult patients with moderate to severe AD who have been chosen to start treatment with abrocitinib in a real-world context such as dermatological practices in Germany. The following factors will be considered, if collected as part of the medical routine:

Primary Objective:

The primary objective of this non-interventional study is to describe the efficacy of abrocitinib treatment.

- *In terms of patients achieving a clear or almost clear AD morphology 3 months after first prescription of abrocitinib based on the IGA Questionnaire.*
- *In terms of patients achieving a ≥75% improvement in lesion extent and severity 3 months after first prescription of abrocitinib based on the EASI.*

Secondary Objectives:

The secondary objectives of this non-interventional study are:

- *To document the efficacy of abrocitinib treatment based on physicians´ assessment:*
  - *Physician's global assessment of AD: Scoring Atopic Dermatitis (SCORAD), EASI, IGA change to baseline.*
- *To document the efficacy of abrocitinib treatment based on patients´ assessment:*
  - *Patient's global assessment of AD: change in quality of life, Dermatology Life Quality-Index (DLQI), Patient Oriented Eczema Measure (POEM);*
  - *Patient´s assessment of anxiety and depression: Hospital Anxiety and Depression Scale (HADS);*
  - *Patient's assessment of pruritus: Peak Pruritus Numeric Rating Scale (PP-NRS), mean-NRS and sleep: Medical Outcomes Study Sleep (MOS) Scale;*
  - *Meeting the patient's expectations (change in the Patient Benefit Index [PBI]) with regard to medical treatment;*
  - *Number of days with topical-treatment use (topical corticosteroid (TCS), topical calcineurin inhibitor (TCI);*
  - *Number of days with emollients use.*

Explorative objectives:

The explorative objectives of this non-interventional study are:

- *To document patient characteristics and treatment decisions in terms of:*
  - *patient characteristics, clinical history, comorbidities and previous therapies;*
  - *reasons for starting/ending treatment with abrocitinib, concomitant treatments;*
  - *dosage and actual use of abrocitinib as assessed by the treating physician and the patient.*
- *To assess the safety in terms of adverse and serious adverse events that will occur in the observation period. Severity categories (mild, moderate and severe) of adverse events will be assessed based on investigator´s assessment (when applicable).*

2 INTERIM ANALYSES

Two interim analyses are planned for this study. Table 3 shows the planned analyses schedule. Results of earlier interim analyses will be updated in each later analysis.

Table 3. Content of Interim analysis

Table 3 Content of Interim Analysis

Analysis	Year	Population cut-off	New Content
Interim analysis 1 (IA1)	Not applicable – see population cut-off	When approximately 15 % of patients completed Visit 1	Baseline characteristics, explorative endpoints as well as usage of abrocitinib and effectiveness at visit 2.
Interim analysis 2 (IA2)	Not applicable – see population cut-off	When approximately 40 % of patients completed Visit 4	Baseline characteristics, explorative endpoints as well as usage of abrocitinib and effectiveness at each available timepoint.
Final analysis	2028	All patients	Patient characteristics, usage and effectiveness, anything not yet analyzed.

Two interim analyses will be carried out. The first interim analysis (IA) will be conducted when approximately 15 % of the planned number of patients have reached their V1 (baseline) visit. The IA1 interim analysis will consider explorative endpoints with focus on baseline characteristics, transition to abrocitinib treatment as well as usage of abrocitinib and effectiveness at visit 2 respectively.
The interim analysis will be repeated (IA2) when approximately 40 % of patients completed visit 4. This interim analysis will consider the same aspects as IA1 and effectiveness at every other available timepoint.

3 FINAL ANALYSES

The final analysis will include all enrolled patients and will be carried out after all patients have reached their final visit (at Month 12). The final datasets will be extracted from the database and locked before final analysis. Any exclusions from the analysis will be agreed and documented prior to database lock.

4 HYPOTHESES AND DECISION RULES

As the protocol states, this is a solely descriptive and explorative non-interventional study with the aim to generate hypothes. In order to generate hypotheses the statistical tests mentioned in section 8.2.3 are carried out for the subgroups defined in section 5.4.

4.1 STATISTICAL HYPOTHESES

Not applicable.

4.2 STATISTICAL DECISION RULES

Not applicable.

5 ANALYSIS SETS/POPULATIONS

5.1 FULL ANALYSIS SET

The Full Analysis Set (FAS) consists of all patients with informed consent who met the eligibility criteria and received at least one dose of abrocitinib.
This population will be used for all analyses except safety.

5.2 SAFETY ANALYSIS SET

The Safety Analysis Set (SAF) consists of all patients with informed consent who received at least one dose of abrocitinib.
This population will be used for safety analysis, i.e. for the analysis of adverse events and laboratory values.

5.3 OTHER ANALYSIS SET

The modified Full Analysis Set (mFAS) consists of all patients who met the eligibility criteria, received at least one dose of abrocitinib and had at least one post-baseline visit.
This population will be used for analysis of primary and secondary endpoints, if ≥ 10% of the FAS is omitted.

The Per Protocol Set (PP) consists of all patients who met the eligibility criteria, received at least one dose of abrocitinib and completed all visits, irrespective of the time-window.

This population will be used for analysis of primary and secondary endpoints, if ≥ 10% of the mFAS is omitted.

5.4 SUBGROUPS

The following subgroups will be analysed:

- Sequence of dosage (50 mg → 100 mg vs. 100 mg → 50 mg vs. 100 mg → 200 mg vs. 200 mg → 100 mg vs. 200 mg vs. 100 mg vs. 50 mg)
- Medication history* (prior conventional systemic treatment, prior biologic, prior JAKi, none of those)
- Dosage switchers (patients who switched from abrocitinib vs. patients who remain on abrocitinib)
- Abrocitinib responder, defined as: EASI-75-responder and/or SCORAD-75-responder and/or IGA 0/1
- EASI-90 responder (yes vs. no)

If less than 20 patients are in one subgroup class, classes will be combined in a meaningful way or the subgroup analysis will be omitted with reason.
*Pfizer will assign the prior medication documented to (i) topical (TCS,TCI,other), (ii) systemic (conventional, biologics, JAKi, other), (iii) phototherapy and (iv) other in order to analyze the pretreatment and form the subgroup "medication history" accordingly.

6 ENDPOINTS AND COVARIATES

All primary and secondary endpoints are based on scales, either assessed by the physician or the patient. Baseline is defined as day 1, the respective time windows for post-baseline visits are given in Table 2.

6.1 EFFICACY/EFFECTIVENESS ENDPOINT(S)

Effectiveness endpoints comprise of all primary and secondary endpoints, i.e. effectiveness, and quality parameters assessed by the physicians and the patients.

Primary endpoint analysis

Variable	Role	Data source(s)	Operational definition
EASI	Primary outcome variable	Case records	Percentage of patients with 75% reduction from baseline in EASI at month 3
IGA	Primary outcome variable	Case records	Percentage of patients with IGA score 0 or 1 at month 3

Secondary endpoint analysis

Variable	Role	Data source(s)	Operational definition
SCORAD	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the total score and SCORAD-A at each point in time, respectively as well as the respective percentage change to baseline
EASI	Secondary outcome variable	Case records	1. Percentage of patients with 75% reduction from baseline in EASI irrespective of the point in time 2. Percentage of patients with 90% reduction from baseline in EASI irrespective of the point in time 3. Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the respective percentage change to baseline
IGA	Secondary outcome variable	Case records	1. Percentage of patients with IGA score 0 or 1 irrespective of the point in time 2. Percentage of patients with IGA score 0 or 1 and a reduction from baseline of ≥2 points irrespective of the point in time 3. Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the respective percentage change to baseline ((score at respective visit – score at baseline)/score at baseline*100)

Pruritus-NRS	Secondary outcome variable	Case records	1. Percentage of patients achieving at least 4 points improvement of Pruritus NRS from baseline 2. Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the percentage change to baseline 3. Percentage of patients with Pruritus NRS ≤1
PP- NRS	Secondary outcome variable	Case records	1. Percentage of patients achieving at least 4 points improvement of PP NRS from baseline 2. Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the percentage change to baseline 3. Percentage of patients with PP NRS ≤1
DLQI	Secondary outcome variable	Case records	1. Percentage of patients achieving at least 4 points improvement of DLQI from baseline 2. Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the percentage change to baseline 3. Percentage of patients with DLQI ≤1
POEM	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time as well as the percentage change to baseline
MOS-Sleep scale	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the

			scales at each point in time as well as the percentage change to baseline
Patient Benefit Index	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the single items and the total score at each appropriate point in time as well as the percentage change to visit 2 (about one months after baseline)
Patient Expectations on and Satisfaction with abrocitinib treatment	Secondary outcome variable	Case records	As measured by PBI questionaire (refer to line above; expectation PBI at baseline, satisfaction PBI at all points in time after baseline)
EQ-5D-5L	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the VAS and EQ-5D index score at each point in time as well as the percentage change to baseline
HADS	Secondary outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the anxiety score and depression score at each point in time, respectively as well as the percentage change to baseline
Number of days with topical treatment use (TCS, TCI)	Secondary outcome variable	Case records	Date of first topical treatment – date of last topical treatment + 1 Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Number of days with emollients use	Secondary outcome variable	Case records	Date of first emollients use – date of last emollients use + 1 Summary statistics (n, mean, median, standard deviation, minimum and maximum)

Analysis of questionnaires

Questionnaire	Analysis
SCORAD	Scoring Atopic dermatitis: validated scoring index for AD for severity, combining A: extent (0-100), B: severity (0-18) and C: subjective symptoms (0-20) based on itching and sleep deprivation, each scored (0-10). The SCORAD for an individual is calculated using the formula A/5 + 7B/2 + C (may range from 0 to 103).
EASI	Eczema Area and Severity Index assesses both clinical signs of AD as well as extent of disease; scores can range from 0 to 72, with higher scores representing greater severity of AD. For "head and neck", "trunk", "upper extremities" and "lower extremities" the extent of eczema is assessed by an area score between 0 and 6, respectively. For each area the severity of "erythema", "edema/papulation", "excoriation" and "lichenification" is scored 0 to 3, respectively. The scores for the signs are added for each area and multiplied by the respective arera score. The EASI for an individual is calculated as weighted sum: 0.1 x score for head/neck + 0.3 x score for trunk + 0.2 x score for upper extremities + 0.4 x score for lower extremities.
IGA	Investigators Global Assessment: assesses the severity of AD (excluding scalp, palms and soles) on a 5-point scale from 0 (clear) to 4 (severe) from the investigator's perspective.
Pruritus-NRS	The NRS is comprised of one item and represents the numbers 0 ("no itch") to 10 ("worst imaginable itch"). Subjects are asked to rate the intensity of their average pruritus using this scale.
Peak-Pruritus-NRS	Numeric rating scale: evaluates itching in the last 24 hours from no itching [0] to worst possible itching [10].
POEM	Patient-oriented Eczema Measure: patient-reported measure that assesses AD symptoms. The patient himself evaluates the frequency of occurrence and severity of 7 symptoms (such as itching and burning of the skin) within the last week, each according to a 5-point Likert scale from 0 ("at no day") to 4 ("at all days"). The severity is summed over the symptoms. The maximum POEM score is 28 points. If one question is missing it is scored with 0 and the scores are summed as described before. If two or more questions are not answered the questionnaire is not scored. If two or more response options are selected, the response option with the highest score should be recorded.
DLQI	The DLQI is a 10-item patient-reported measure that rates how much a patient´s skin problems have affected their life over the last week assigned to the following 6 dimensions: symptoms, daily life, leisure/sport, work/school, social life/relationship and abrocitinib treatment. For each question, 0 to 3 points are given, whereby 3 points indicate the greatest possible impairment of the QoL in the queried area. The sum of scores ranges from 0 to 30, with higher scores indicating greater impairment of quality of life. If one question is unanswered it is scored with 0. If more than one question is not answered the score cannot be determined. (https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index)
MOS	The Medical Outcomes Study Sleep Scale (MOS-Sleep) includes 12 items assessing sleep disturbance (questions 1, 3 (R-reversed), 7 (R) and 8(R)), sleep adequacy (questions 4 (R) and 12 (R)), somnolence (questions 6 (R), 9(R) and 11 (R)), quantity of sleep (question 2), snoring (question 10 (R)), and awakening short of breath or with a headache (question 5 (R)) whereat question 1 scores from 1 (0-15 min) to 5 (>60 min) and questions 3 to 12 from 1 (all of the time) to 5 (none of the time). 1 is recoded to 0, 2 to 25, 3 to 50, 4 to 75 and 5 to 100. If the answers have to be reversed 1 is recoded to 100, 2 to 75, 3 to 50, 4 to 25 and 5 to 0. The scores represent the average for all items in the scale that were answered, i.e. missing data are not taken into account.
PBI	Measurement of patient defined treatment benefits according to German and international standards, contains two one-sided questionnaires which are to be completed by the patient before and after receiving a treatment. A total of 25 possible treatment goals are evaluated on an importance scale from 0 ("not at all") to 5 ("very"). "does not apply to me" will be coded as "0". The analysis will include: a) means and standard deviations of all items („does not apply to me" is coded as 0 for this single-item analysis of the PBI) b) for each item the percentage of the response „does not apply to me" c) for each item the percentage of responses with high agreement (quite or very) d) percentage of missing values The weighted index value, the actual "Patient Benefit Index" (PBI), is calculated by multiplying the achieved benefits (respective PBI after baseline) with the importance of the respective needs prior to therapy (PBI at baseline), dividing these products by the sum of all importance items (PBI at baseline), and summing them up for all items. The total PBI score ranges from 0 (no benefit) to 5 (maximal benefit).

EQ-5D-5L	Generic instrument for measuring quality of life, including health benefits and health status on a visual analogue scale (VAS), using the five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). The health status is given as a sequence of the five diemnsions.Missing values are coded as "9". However the EQ-5D index score can only be determined according to the EQ-5D-5L German values if all 5 health dimensions have been specified.
HADS	The Hospital Anxiety and Depression Scale is a 14-item measure that identifies anxiety (7 items) and depression (7 items) among adults who are physically ill with lower scores indicating lower levels of anxiety and depression. Scoring for each item ranges from 0 to 3, with 3 denoting highest anxiety or depression level. For both subscales the score is derived by summing up the respective 7 items.

6.2 SAFETY ENDPOINTS

Incidence and severity of all adverse events including serious adverse events (SAEs).

The reporting of safety data will be in accordance with Pfizer Data Standards.

Variable	Role	Data source(s)	Operational definition
Occurrence of adverse events	Safety outcome	Case records	Number and percentage of SOC and PT according to maximal grade of adverse event (patient based)
Occurrence of adverse drug reactions	Safety outcome	Case records	Number and percentage of SOC and PT according to maximal grade of adverse drug reaction (patient based)
Occurrence of serious adverse events	Safety outcome	Case records	Number and percentage of SOC and PT according to maximal grade of serious adverse event (patient based)
Occurrence of serious adverse drug reactions	Safety outcome	Case records	Number and percentage of SOC and PT according to maximal grade of serious adverse drug reaction (patient based)
Reason for seriousness	Safety outcome	Case records	Number and percentage for each reason (event based)
Occurrence of scenarios involving drug exposure	Safety outcome	Case records	Number and percentage (patient based)
Reason for scenario involving drug exposure	Safety outcome	Case records	Number and percentage for each reason (event based)
Worst outcome	Safety outcome	Case records	Number and percentage (patient based), order: recovered,

			recovered with sequelae, not recovered, unknown, fatal
Action taken	Safety outcome	Case records	Number and percentage for each reason (event based)
Type and results of performed laboratory checks	Potential confounder, potential subgroup identifier, safety outcome	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the minimal and maximal value per patient, respectively

6.3 OTHER ENDPOINTS

Variable	Role	Data source(s)	Operational definition
AD-treatment with abrocitinib and/or without topicals – total days	Exposure, Potential confounder, potential subgroup identifier	Case records	Date of last treatment – date of first treatment +1 Summary statistics (n, mean, median, standard deviation, minimum and maximum)
AD-treatment with abrocitinib and/or without topicals – stratified by abrocitinib dose	Exposure, Potential confounder, outcome, potential subgroup identifier	Case records	Date of last treatment – date of first treatment +1 Summary statistics (n, mean, median, standard deviation, minimum and maximum) stratified by the abrocitinib dose most often applied during the study
Age (Year of birth)	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Age=year of IC – year of birth Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Sex	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
Height	Baseline characteristics	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Weight	Baseline characteristics	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Highest level of education	Baseline characteristics, potential confounder	Case records	Frequency analysis
Ethnicity	Baseline characteristics	Case records	Frequency analysis

Occupational status	Baseline characteristics	Case records	Frequency analysis
Alcohol consumption status	Baseline characteristics, potential confounder	Case records	Frequency analysis
Insurance type	Baseline characteristics	Case records	Frequency analysis
Presence of family history of atopic diseases	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
History of herpes simplex and/or eczema herpeticum and/or herpes zoster	Baseline characteristics	Case records	Frequency analysis
Vaccination status (Herpes zoster, Covid-19, Influenza Varicella)	Baseline characteristics	Case records	Frequency analysis
Age at initial diagnosis of AD	Baseline characteristics, potential confounder	Case records	Age at initial diagnosis =year of initial diagnosis – year of birth 1. Summary statistics (n, mean, median, standard deviation, minimum and maximum) 2. Categorical: < 12 y, 12- < 18 y and ≥ 18 y
Smoking history and current smoking status	Baseline characteristics, potential confounder	Case records	Frequency analysis
Renal and/or liver impairment	Baseline characteristics	Case records	Frequency analysis
Comorbidities at baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
If positive anamnesis at baseline exists: Improvement of (allergic) asthma symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
If positive anamnesis at baseline exists: Improvement of (allergic) rhinitis symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
If positive anamnesis at baseline exists: Improvement of polyposis nasi symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
If positive anamnesis at baseline exists: Improvement of alopecia areata from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis

If positive anamnesis at baseline exists: Improvement of chronic hand eczema symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
If positive anamnesis at baseline exists: Improvement of prurigo nodularis symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
Previous treatments for diagnosed AD	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Frequency analysis
Concomitant treatment of AD (and dosage)	Baseline characteristics, Exposure, explorative outcome, potential confounder, potential subgroup identifier	Case records	Frequency analysis and Summary statistics (n, mean, median, standard deviation, minimum and maximum) for dose
Concomitant (non-AD) treatment	Baseline characteristics, outcome, potential confounder, potential subgroup identifier	Case records	Frequency analysis with respect to level 1 and level 2 of ATC codes
Dosage of abrocitinib used	Exposure, potential confounder, explorative outcome variable, potential subgroup identifier	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Compliance with abrocitinib treatment (patients´ reported compliance)	potential confounder, explorative outcome	Case records	Frequency analysis
Reasons for start of abrocitinib therapy	Explorative outcome variable	Case records	Frequency analysis
Reasons for prescribed dose of abrocitinib therapy	Explorative outcome variable	Case records	Frequency analysis
Reasons for discontinuation of abrocitinib therapy	Explorative outcome variable	Case records	Frequency analysis
Number of flares	Explorative outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Number of hospitalizations due to AD	Explorative outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)
Number of absent days at work/study due to AD	Explorative outcome variable	Case records	Summary statistics (n, mean, median, standard deviation, minimum and maximum)

6.4 COVARIATES

Not applicable.

7 HANDLING OF MISSING VALUES

In general, no imputation of missing data will be performed. Exceptions are described below. For categorical variables the number of missing values will be displayed in the respective tables. For at least interval-scaled variables the number of available observations will be displayed.
Incomplete dates will be handled as follows, if not specified otherwise:
If the day of a date is missing then the day is set to the 15th of the respective month. If day and month are missing then the date will be set to the middle of the respective year (in case of the year of the data cut: middle of time from beginning of year to data cut).

Missing values in PRO will be replaced according to the respective manual.

8 STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

8.1 STATISTICAL METHODS

All parameters will be evaluated in a descriptive respective explorative manner. Binary, categorical and ordinal parameters will be summarized by means of absolute and percentage numbers within the various groups (including 'missing data' as valid category). Those variables will be compared for the subgroups in an explorative manner using Chi-Square test respective Fisher's exact test if a sample size of at least 30 in each subgroup is not reached. Numerical data will be summarized by means of standard statistics (i.e. number of available data, number of missing data, mean, standard deviation, minimum, median and maximum) and compared exploratively for the subgroups by Mann-Whitney-U-test. Due to the descriptive/explorative manner of the analysis no adjustment for multiple testing will take place. Graphical displays may be used.

8.2 STATISTICAL ANALYSES

Due to the nature of the study data, descriptive statistics will be used to summarize all endpoints. Tests for subgroup analyses are purely explorative.

8.2.1 Safety Analyses

Treatment-emergent adverse events are adverse events which worsen or start after start of treatment with abrocitinib but no later than 28 days after end of treatment with abrocitinib.
In addition to the analysis of treatment-emergent adverse events and drug-related adverse events as specified in 6.2 adverse events which occurred under another systemic treatment, following cessation of abrocitinib, will be given and presented in a separated listing. Number and percentage of SOC and PT will be presented according to maximal grade.

8.2.2 Analyses of endpoints

Please refer to the "operational definition" in section 6.1 and 6.3.

8.2.3 Summary of Analyses

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale) at month 3	FAS, mFAS, PP	1	All	Percentage of patients with IGA score 0 or 1 at month 3 Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Response based on achieving the EASI-75 at month 3	FAS, mFAS, PP	2	All	Percentage of patients with 75% reduction from baseline in EASI at month 3 Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale)	FAS, mFAS, PP	3	All	Percentage of patients with IGA score 0 or 1 irrespective of the point in time Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Response based on achieving the EASI-75	FAS, mFAS, PP	4	All	Percentage of patients with 75% reduction from baseline in EASI irrespective of the point in time Chi-Square test respective Fisher's exact test for subgroups	None	Excluded

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
Response based on achieving the EASI-90	FAS, mFAS, PP	5	All	Percentage of patients with 90% reduction from baseline in EASI irrespective of the point in time Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Response based on achieving the IGA of clear (0) or almost clear (1) and a reduction from baseline of ≥2 points	FAS, mFAS, PP	6	All	Percentage of patients with IGA score 0 or 1 and a reduction from baseline of ≥2 points irrespective of the point in time Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Percentage change of IGA compared to baseline	FAS, mFAS, PP	7	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Percentage change of SCORAD compared to baseline	FAS, mFAS, PP	8	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Absolute EASI values over time	FAS, mFAS, PP	9	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time	None	Excluded

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
				Mann-Whitney-U test for subgroups		
Percentage change of EASI compared to baseline	FAS, mFAS, PP	10	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Absolute change of IGA compared to baseline	FAS, mFAS, PP	11	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) of the score at each point in time Mann-Whitney-U test for subgroups	None	Excluded
Response based on achieving at least 4 points improvement of Pruritus NRS from baseline and patients with Pruritus NRS ≤1	FAS, mFAS, PP	13	All	Percentage of patients achieving at least 4 points improvement of Pruritus NRS from baseline Percentage of patients with Pruritus NRS ≤1 Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Response based on achieving at least 4 points improvement of PP NRS from baseline and patients with PP NRS ≤1	FAS, mFAS, PP	14	All	Percentage of patients achieving at least 4 points improvement of PP NRS from baseline Percentage of patients with PP NRS ≤1 Chi-Square test respective Fisher's exact test for subgroups	None	Excluded

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
Change of Peak-Pruritus NRS over time	FAS, mFAS, PP	15	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Change of POEM from baseline	FAS, mFAS, PP	15	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Change of MOS from baseline	FAS, mFAS, PP	17	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Response based on achieving at least 4 points improvement of DLQI from baseline and patients with DLQI ≤1	FAS, mFAS, PP	18	All	Percentage of patients achieving at least 4 points improvement of DLQI from baseline Percentage of patients with DLQI ≤1 Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Change of DLQI from baseline	FAS, mFAS, PP	19	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Change of HADS from baseline	FAS, mFAS, PP	20	All	(score at respective visit – score at	None	Excluded

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
				baseline)/score at baseline*100 Mann-Whitney-U test for subgroups		
Change of EuroQol five-dimensional-five level (EQ-5D-5L) from baseline	FAS, mFAS, PP	21	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Change of PBI from baseline	FAS, mFAS, PP	22	All	(score at respective visit – score at baseline)/score at baseline*100 Mann-Whitney-U test for subgroups	None	Excluded
Patient's satisfaction with treatment (PBI after baseline)	FAS, mFAS, PP	23	All	Frequency tables for satisfaction with effectiveness and tolerability Chi-Square test respective Fisher's exact test for subgroups	None	Excluded
Number of days with topical-treatment use (TCS, TCI)	FAS, mFAS, PP	24	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) Mann-Whitney-U test for subgroups	None	Excluded
Number of days with emollients use	FAS, mFAS, PP	25	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum)	None	Excluded

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroups	Statistical Method	Covariates/ Strata	Missing Data
				Mann-Whitney-U test for subgroups		
AD-treatment with abrocitinib and/or without topicals – total days	FAS, mFAS, PP	26	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) Mann-Whitney-U test for subgroups	None	Excluded
AD-treatment with abrocitinib and/or without topicals – stratified by abrocitinib dose	FAS, mFAS, PP	27	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) Mann-Whitney-U test for subgroups	None	Excluded
Number of flares	FAS, mFAS, PP	28	All	Summary statistics (n, mean, median, standard deviation, minimum and maximum) Mann-Whitney-U test for subgroups	None	Excluded

All explorative endpoints mentioned in section 6.3 will be analyzed for FAS and all subgroups, respectively. Safety enpoints , as given in section 6.2 will be analyzed for SAF.

9 LIST OF TABLES AND TABLE SHELLS

For the table shells and the corresponding list of tables, listings and figures of final analysis please refer to the final version of B7451089_Mockups.docx.

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11 APPENDICES

11.1 APPENDIX 1: DATA DERIVATION DETAILS

EASI-75-responder: Percentage of patients with 75% reduction from baseline in EASI
EASI-90-responder: Percentage of patients with 90% reduction from baseline in EASI
SCORAD-75-responder: Percentage of patients with 75% reduction from baseline
Abrocitinib responder: EASI-75-responder and/or SCORAD-75-responder and/or IGA 0/1
Number of days with topical treatment use (TCS, TCI): Date of first topical treatment – date of last topical treatment + 1
Number of days with emollients use: Date of first emollients use – date of last emollients use + 1
Days of AD-treatment: Date of last AD treatment – date first_AD-treatment + 1
Age [years]: Year of informed consent – year of birth
Age at initial diagnosis of AD [years]: year of initial diagnosis – year of birth
Percentage change to baseline: (score at respective visit – score at baseline)/score at baseline*100

Information of additional documentation timepoints will be added to the information of the next scheduled visit and analyzed at the scheduled visit.
PROs and other questionnaires referring to additional documentation timepoints will not be analyzed but may be of interest if the course of individual patients is considered in more detail.

PROs will be assigned to the month/scheduled visit according to the time windows given below.

A1.1 Definition and use of visit windows in interim analysis

Visit Label	Endpoint	Definition [Day window]
Enrolment	All	1
Month 1	All	2 to 44
Month 3	All	45 to 105
Month 6	All	106 to 210
Month 9	All	211 to 301
Month 12	All	302 to 393

A1.2 Further definition of endpoints

11.2 APPENDIX 2: ADDITIONAL STATISTICAL METHODOLOGY DETAILS

Not applicable

A2.1 Further Details of the Statistical Methods

Not applicable