NON-INTERVENTIONAL STUDY PROTOCOL

Study Information

Title	This is a 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)
Protocol number	B7451089
Protocol version identifier	Version 3.0
Date	29 September 2023
Active substance	Janus kinase (JAK)1 Inhibitor Abrocitinib ATC code: D11AH08
Medicinal product	CIBINQO®
Research question and 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.
Author	PPD Pfizer Pharma GmbH Linkstraße 10, D-10785 Berlin

1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AD	Atopic dermatitis
AE	Adverse event
AEM	Adverse event monitoring
AMG	Medicinal Products Act
ATP	Adenosine Triphosphate
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte (German Federal Institute for Drugs and Medical Devices)
BSA	Body Surface Area
CI	Confidence Interval
CIOMS	Council for International Organizations of Medical Sciences
CRA	Clinical Research Associate
CRO	Clinical Research Organization
CSA	Cinical Study Agreement
DLQI	Dermatology Life Quality-Index
EASI	Eczema Area and Severity-Index
eCRF	Electronic case report form
EDP	Exposure During Pregnancy
EMA	European Medicines Agency
EoS	End of Study
EQ-5D-5L	EuroQol five-dimensional-five level

Abbreviation	Definition
FSA	Voluntary Self-Regulation for the Pharmaceutical Industry
GEP	Good Epidemiological Practice
GPP	Good Pharmacoepidemiology Practice
HADS	Hospital Anxiety and Depression Scale
HCP	Healthcare Professional
IEA	International Epidemiological Association
IEC	Independent Ethics Committee
IGA	Investigators Global Assessment
IL	Interleukin
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JAK	Januskinase
MoA	Mechanism of Action
MOS	12-item Sleep Scale from the Medical Outcomes Study
NIS	Non-Interventional study
NRS	Numerical Rating Scale
PBI	Patient Benefit Index
PC	Personal Computer
PEI	Paul-Ehrlich Institute

Abbreviation	Definition
POEM	Patient Oriented Eczema Measure
PP-NRS	Peak Pruritus Numeric Rating Scale
PRO	Patient reported outcome
QD	Once Daily
QoL	Quality of Life
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCORAD	Scoring Atopic Dermatitis
SmPC	Summary of Product Characteristics
TCI	Topical Calcineurin Inhibitor
TCS	Topical Corticosteroid
Th2	Type 2 helper T
TYK2	Tyrosine Kinase 2
VAS	Visual Analogue Scale
VfA	Verband der forschenden Pharma-Unternehmen (German association of research-based pharmaceutical companies)

3. RESPONSIBLE PARTIES

3.1. Sponsor

Pfizer Pharma GmbH
Linkstraße 10
D-10785 Berlin
Germany

3.2. Principal Investigator(s) of the Protocol

Name, degree(s)	Job Title	Affiliation	Address
Athanasios Tsianakas, PD Dr. med.	Coordinating Investigator	Fachklinik Bad Bentheim Abt. für Dermatologie und Allergologie	Am Bade 1 48455 Bad Bentheim Germany
Laurens Neumann.	Medical Affairs Scientist Field	Pfizer Pharma GmbH	Linkstraße 10 10785 Berlin Germany

3.2.1. Contributors to the Protocol

Name, degree(s)	Job Title	Affiliation	Address
PPD MD Dr. med.	PPD	Pfizer Pharma GmbH	Linkstraße 10 10785 Berlin Germany
PPD PhD		Pfizer Pharma GmbH	Linkstraße 10 10785 Berlin Germany
PPD PhD		Pfizer Pharma GmbH	Linkstraße 10 10785 Berlin Germany
PPD MD Dr. med.		Pfizer Pharma GmbH	Linkstraße 10 10785 Berlin Germany
PPD PPD Dr.		Alcedis GmbH	Winchesterstr. 3 35394 Gießen Germany
PPD Dr.		Alcedis GmbH	Winchesterstr. 3 35394 Gießen Germany

4. ABSTRACT

Not applicable.

5. AMENDMENTS AND UPDATES

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
2	15-Feb-2022	administrative	3, 6, 9, 10	Change of job title. Start of data collection 15 April 2022. Adding milestones and dates of interim analyses. Clarify that patients who are unable to consent will not be included in this study.	Administrative change of job title, updates of milestones (start of data collection and interim analyses), clarification of patients who are unable to consent in exclusion criteria and in patient consent according to recommendation of ethics commission.
3	04-Aug-2023	substantial	2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, Annex 1, Annex 2, Annex 3	2: Correction of translation error. Correction of spelling. Addition of the abbreviations “AdV” and “EoS” to the list of abbreviaitons. Removal of “HCP”.	English translation of “AMG” was incorrect. See summary. See summary. Because of word harmonization “HCP” is not used any more.
				3: Changes in study roster and job titles.	NI-Study Lead changed, as well as removal of the project manager of the CRO, since project manager was added errantly to the contributions list. Role of PPD PPD rephrased since PPD does not partake in study conduction.
				4: Removal of the abstract.	As abstract is not necessary, it was removed to streamline the outline of the protocol.
				5: Amendments	Update to the Summary of changes since several sections were updated.

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				6: Alignment of Milestones to actual study start, prolongation of the recruitment phase, and adaptation of interim analyses to be triggered by number of applicable patients only. Updating dates of start and end of data collection, and final study report.	Slow recruitment pace does not allow to adhere to initial timelines. To avoid a negative impact on interim analyses, the interim analyses will only be triggered by the number of applicable patients only rather than a fixed date. Since date of FPFV is known all connected dates are updated as well.
				7: Correction of spelling and phrasing. Update to the study rationale and clarified that "first prescription" means "first prescription after inclusion in this oberservational study".	See summary. Rephrasing also to clarify that abrocitinib experienced patients may also be included. Updated to give scientific rationale to the enhanced endpoint (see Section 9). "First prescription" was clarified so that abrocitinib experienced patients may be included as well.
				8: Correction of spelling and phrasing. Removal of the endpoint physician's satisfaction and expectation. Clarification that patient's expectation and satisfaction with treatment will be assessed with the PBI.	See summary. Initial setup of eCRF was conducted without implementation of the endpoint physician's expectation. As these endpoints are not validated, both endpoints will be removed as no scientific benefit can be inferred from it. This endpoint is captured twice as validated PRO and as unvalidated standalone question in the eCRF. Doubled capturing was deemed unnecessary and the validated endpoint was chosen while the unvalidated was removed.

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				9: Correction of spelling and phrasing.	See summary. Rephrasing also to clarify that abrocitinib experienced patients may also be included.
				Exchanged endpoint 3b with 3g	Endpoints were the same and therefore one was redundant.
				Removal of the endpoint physician's satisfaction and expectation.	Initial setup of eCRF was conducted without implementation of the endpoint physician's expectation and satisfaction. As both endpoints are not validated, the endpoint will be removed as no scientific benefit can be inferred from it
				Enhancement of the comorbidity endpoints	Enhancing the endpoint "comorbidities of interest" to include a qualitative outcome assessment for alopecia areata, allergic rhinits, asthma, chronic hand eczema, nasal polyps and prurigo nodularis. Scientific rationale was added in Section 7.4
				Prolongation of the recruitment phase and administrative changes resulting out of this.	Slow recruitment pace interferes with planned timelines and study design
				Updated start study start.	Update because actual date is known now.

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				9 (continued) Administrative changes due to new version of CT24-WI-GL02-RF01 4.0	Updated template (CT24-WI-GL02-RF01 6.0)
				Clarification of the inclusion and exclusion criteria to be more concise on the aspect that abrocitinib naïve and experienced patients can be enrolled as well as clarified the time periods.	Misunder-standings regarding the enrollment of abrocitinib naïve and experienced patients as well as uncertainity over the time periods.
				Renaming “schedule of activities” to “recommended schedule of activities”.	To avoid intervention and clarify that visits are oriented solely upon clinical routine the "schedule of activities” was rephrased to “recommended schedule of activitities”.
				Clarification that patient’s expectation and satisfaction with treatment will be assessed with the PBI.	This endpoint is captured twice as validated PRO and as unvalidated standalone question in the eCRF. Doubled capturing was deemed unnecessary and the validated endpoint was chosen while the unvalidated was removed.
				Clarification that certain endpoints will be observed even after treatment with abrocitinib is discontinued	See summary

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				9. (continued) Updated Table 2 due to the further specification of endpoints as well as administrative changes to use more concise language. Updating the usage of paper-based questionnaire to patient preference. Includes administrative changes regarding this update. Differentiation of the phrase “Electronic plausibility checks” Clarification that eCRF serves as source document for the patient questionnaires. Updated monitorings to include remote monitorings as well. Also follow-up letters are added to the process and monitorings are announced to the sites in advance.	See summary. Difficulties of patients using the tablet PC for ePROs “Edit checks” and “electronic plausibility checks” are more concise. See summary. See summary

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				10: Administrative changes. Correction of wrong translation of "AMG", spelling, and phrasing. Clarified that treatment discontinuation does not constitute patient withdrawal.	See summary. See summary.
				11: Administrative changes. Correction of spelling and phrasing. Updated Safety Language text; deletion of "Protocol-specified admission during clinical study (eg, for a procedure required by the study protocol)". Added a caption for table 3. Clarification of the safety reporting periods. Clarification to the reporting requirements of pregnancies (Annex 1).	See summary. Safety Language text was updated from CT24-WI-GL02-RF01A 2.0 to CT24-WI-GL02-RF01A 3.0. See summary. Unconcise language regarding reporting periods suggesting 24 h reporting period for non-serious adverse events. Uncertainties to the reporting process.
				12: Adding references and harmonizing citation style.	See summary. Some references were updated due to incoherent citation style.
				13: Adding hyperlinks and page numbers. Added a title of table 3.	See summary.

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section Changed	Summary of Amendment(s)	Reason
				Annex 1: Adding the document B7451089_Pregnancy Reporting Process_V1_16JUN2023 to the list. Removal of Abstract from list of "List of stand alone documents".	Uncertainties to the reporting process. See above, section 4.
				Annex 2: Removal of Annex 2	Removal due to updating template CT24-WI-GL02-RF01 4.0 to CT24-WI-GL02-RF01 6.0
				Annex 3: Renamed Annex 3 to Annex 2	Removal of Annex 2.

6. MILESTONES

Milestone	Planned date
Start of data collection	10 May 2022
Interim Report 1	When approximately 15 % of patients completed Visit 1
Interim Report 2	When approximately 40 % of patients completed Visit 4
End of data collection	31 May 2027
Final study report	30 April 2028

7. RATIONALE AND BACKGROUND

7.1. Atopic Dermatitis

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.

7.2. 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.

7.3. 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]

7.4. 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 (ie, 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.

8. RESEARCH QUESTION AND 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:

Research Questions:

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-75.

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).

9. RESEARCH METHODS

9.1. 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 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.

9.1.1. Endpoints

Primary Endpoints:

a. Response based on achieving the **IGA** of clear (0) or almost clear (1) (on a 5-point scale) at month 3.

b. Response based on achieving the **EASI-75** at month 3.

Secondary Endpoints:

Physician´s global assessment of efficacy parameters (assessed at all visits [except for month 3 for a. and b.]):

a. Response based on achieving the **IGA** of clear (0) or almost clear (1) (on a 5-point scale).

b. Percentage of patients with **EASI-75** response compared to baseline.

c. Response based on achieving the **EASI-90.**

d. Response based on achieving the **IGA** of clear (0) or almost clear (1) and a reduction from baseline of ≥2 points.

e. Percentage change of **IGA** compared to baseline.

f. Percentage change of **SCORAD** compared to baseline.

g. Absolute **EASI** values over time.

h. Percentage change of **EASI** compared to baseline.

i. Absolute change of **IGA** compared to baseline.

Patient´s assessment of efficacy and quality parameters (assessed at all visits):

a. Response based on achieving at least 4 points improvement of Pruritus **NRS** from baseline.

b. Change of Peak-Pruritus **NRS** over time.

c. Change of **POEM** from baseline.

d. Change of MOS from baseline.

e. Change of DLQI from baseline.

f. Change of HADS from baseline.

g. Change of EuroQol five-dimensional-five level (EQ-5D-5L) from baseline.

h. Patient's satisfaction with treatment measured by PBI.

i. Patient's expectation of treatment measured as PBI at baseline.

j. Number of days with topical-treatment use (TCS, TCI).

k. Number of days with emollients use.

Explorative Endpoints:

Treatment characteristics (assessed at all visits):

a. Concomitant treatments.

b. Tolerability of abrocitinib and reasons for discontinuation.

c. Dosage of abrocitinib.

d. Compliance with abrocitinib treatment.

Patient characteristics assessed at baseline visit only (except for c., f., g., and h. with additional assessment at subsequent visits):

a. Demographic data of patient (age, sex, weight, occupation, alcohol/smoking, family history).

b. Clinical history of AD treatment before non-interventional study start.

c. Comorbidities of interest (atopic diseases, malignancies, cardiovascular diseases, alopecia areata, prurigo nodularis, hand eczema). If baseline visit had a positive anamnesis for the following: (allergic) asthma, (allergic) rhinitis, polyposis nasi, chronic hand eczema, prurigo nodularis and alopecia areata, a qualitative outcome assessment will be done (ie, assessment of investigator if comorbidity improves during abrocitinib therapy).

d. Previous therapies and reasons for termination of previous treatments.

e. Reasons for starting treatment with abrocitinib.

f. Number of AD flares one year before start of treatment with abrocitinib and during observational period.

g. Number of absent days at work/study caused of AD one year before start of treatment with abrocitinib and during observational period.

h. Number of AD hospitalizations in the observation period and one year before start of treatment with abrocitinib.

Documentation of safety:

a. Safety: incidence of adverse events and serious adverse events.

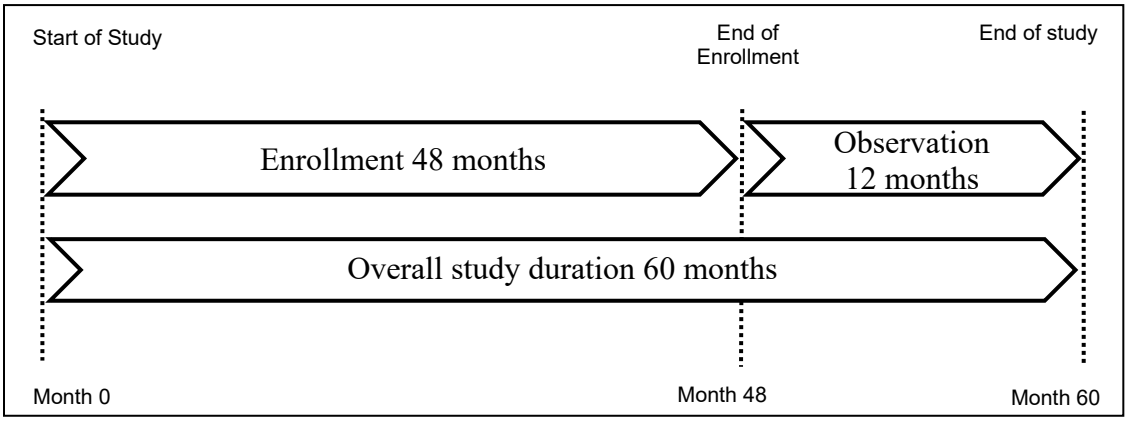
b. Severity of adverse events (when applicable) (as assessed by the investigator according to the following categories:

- Mild: Does not interfere with the patient´s usual function.
- Moderate: Interferes to some extent with the patient´s usual function.
- Severe: Interferes significantly with the patient´s usual function.

9.2. Study Setting

Figure 1. Timelines

In total, this non-interventional study aims to enroll at least 750 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.



9.2.1. Inclusion Criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in the non-interventional study:

1. Patients aged ≥18 years.
2. Confirmed diagnosis of AD by dermatologist prior to study inclusion.
3. Patient for whom the decision to initiate treatment with abrocitinib was made as part of routine clinical practice irrespective of the patient being
    a. abrocitinib naïve or,
    b. Patients who reinitialize treatment with abrocitinib after being off treatment for ≥28 days prior to study inclusion.
4. Patient is eligible for abrocitinib treatment according to SmPC.
5. Evidence of a personally signed and dated informed consent document indicating that the patient has been informed of all pertinent aspects of the non-interventional study.

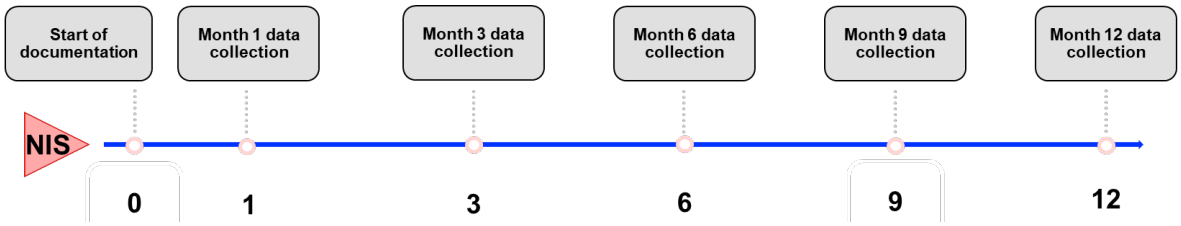
9.2.2. Exclusion Criteria

1. Patients meeting any of the following criteria will not be included in the non-interventional study: Contraindications according to SmPC.
2. Receipt of any investigational drug within 3 months or longer if required according to wash-out period prior to inclusion or participation in a clinical trial during observation period.
3. Patients being treated with abrocitinib within a time period of <28 days prior to the timepoint of study inclusion.
4. Patients who are investigational site staff members or patients who are Pfizer employees directly involved in the conduct of the non-interventional study.
5. Patient who are unable to consent.

9.2.3. Study Period

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



9.2.3.1. Study Procedure

After contractual agreement and ethics committee approval, but before the start of the observational study at a respective site, the study team at this site will be informed in detail about the planned conduction of the NIS, the study objectives, the handling of the electronic case report form (eCRF), the documentation of safety events and all other relevant aspects. This will be done by the delegated Clinical Research Organization (CRO) (Alcedis GmbH, Gießen, Germany) via an online initiation. In addition, each participating site will receive a study binder containing all necessary and essential documents and information. In addition, each site will be provided with a tablet personal computer (PC) which is to be used solely for allowing patients to document the patient questionnaires as outlined in Section 9.2.3.2 (Schedule of Activities) and needs to be returned to the CRO after the end of the study. Afterwards, the trained site staff will get access to the study´s eCRF, where the data and findings of the patient are documented.

Following site initiation, the study site will be open for enrollment of patients. Patients can be included by the investigator if they fulfill all inclusion criteria and do not meet any of the exclusion criteria for the study and are started on treatment with abrocitinib for moderate to severe atopic dermatitis. Within this non-interventional study 6 visits may be documented. All visits shall be scheduled according to clinical practice. The treatment decision to initiate abrocitinib as well as the treatment of a patient itself is independent from the patient´s enrollment into the NIS and carried out as per standard of care. To provide accurate information regarding the treatment, the initial abrocitinib dose and all changes and the reasons for changes are documented during the course of the evaluation. The concomitant treatment of atopic dermatitis is determined by the investigator.

Eligible patients must be informed orally and in written form about the nature and purpose of this non-interventional study by the investigator. After the patient has signed and dated the informed consent, the patient can be enrolled in the NIS.

For each patient a unique patient number is generated automatically in the eCRF to ensure pseudonymized data collection. No direct identifiers like patient names, patient initials or specific birth dates will be documented in the eCRF.

To allow source data verification during quality assurance visits, the patient´s name, address and unique study-specific patient number will be listed in a patient identification list at the respective site. The patient identification is to be kept strictly confidential.

Since patients are to complete the patient questionnaires via the tablet PC provided at the study site, participating patients will receive individual access data to gain access to the questionnaires. The access data for the respective patient of a site can be generated within the eCRF and will be handed out to the patient by the site staff. However, paper-based questionnaires are available as back up for patients that do not want to use the online version or in case of technical issues (eg, internet problems at a study site). If a patient fills out paper questionnaires, these will be sent by mail to the delegated CRO where the data will be entered into the eCRF by qualified and trained personnel.

9.2.3.2. Schedule of Activities

The recommended schedule of activities table provides an overview of the visits that may be documented. Refer to Section 9.2.4 Assessments section of the protocol for detailed information on each documentation and assessment. 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, 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					
Previous treatments for diagnosed AD	X					
Current comorbidities of interest (atopic diseases, malignancies, cardiovascular diseases)	X					
If positive anamnesis at baseline exists: Improvement of asthma symptoms from baseline						X

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
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: Improvement of hand eczema from baseline						X
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	X	X	X	X	X	X

* This includes patients who discontinued treatment with Abrocitinib.

Study period based on routine visits	**Baseline (Enrollment)**	**Month 1**	**Month 3**	**Month 6**	**Month 9**	**Month 12 End of Study (EoS)**
(regardless of Abrocitinib treatment status*)						
Reasons for start of therapy with Abrocitinib	X					
Reasons for discontinuation of therapy with Abrocitinib		X	X	X	X	X
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

* This includes patients who discontinued treatment with Abrocitinib.

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

9.2.4. Assessments

9.2.4.1. Demographic Data

At the baseline Visit (Visit 1) age, sex, weight, height, ethnicity, smoker/non-smoker, education, occupation, alcohol consumption and insurance type (statutory and private health insurance) will be documented.

9.2.4.2. Disease Characteristics and Previous AD Treatments

At the baseline Visit (Visit 1) the presence of a family history of atopic diseases as well as a patient´s clinical history regarding herpes simplex, herpes zoster, eczema herpeticum will be documented. Furthermore, the age at initial diagnosis of AD, previous treatments for diagnosed AD as well as current comorbidities of interest (atopic diseases: asthma, allergic rhinitis, food allergies, nasal polyps; malignancies, cardiovascular diseases) and concomitant non-AD specific treatments will be documented. At the baseline visit the number of flares as well as the number of hospitalizations and the number of absent days at work/study caused by AD during the last 12 months prior to start of abrocitinib will be documented. At each of the subsequent visits (Visit 2-6), the number of flares, the number of hospitalizations due to AD, as well as the number of absent days at work/study since the last documented visit will be captured.

9.2.4.3. Vaccination Status

At the baseline Visit (Visit 1) current vaccination status of patients will be assessed. Further vaccinations against Herpes Zoster, Covid-19, Influenza and Varicella will be assessed. At Visit 6 (Month 12) assessment of vaccination status of patients against Herpes Zoster, Covid-19, Influenza and Varicella in case complete vaccination status was not achieved at baseline visit.

9.2.4.4. Laboratory Checks

At each visit (Visit 1-6) the conduct (yes/no) and the respective value and test date (if applicable) of laboratory checks of the following parameters will be documented. Please note that no laboratory tests need to be performed for study purposes. Only the date of examination and the respective value of laboratory parameters that were routinely collected anyway should be documented. Relevant parameters:

- Complete blood count including platelet count, absolute lymphocyte count, absolute neutrophil count;
- Hemoglobin;
- Lipid parameters.

9.2.4.5. Treatment of Atopic Dermatitis with Abrocitinib

At the baseline visit (Visit 1) reason of starting or re-starting treatment with abrocitinib will be documented. At each visit (Visit 1-6) dose of treatment with abrocitinib and reason for its choice will be documented. If an escalation or a de-escalation of dosage occurred since the last visit, in addition stop date of previous dosage, start date of new dosage and reason for switch (lack of efficacy or intolerability) will be documented.

If treatment with abrocitinib got terminated since the last visit, reasons for ending abrocitinib treatment, stop date of treatment, start date of other new treatment and reason for switch (lack of efficacy or intolerability) will be documented.

At Visits 2-6, the investigator will ask the patient for his or her self-assessment of compliance in terms of number of abrocitinib-free days since the last visit.

9.2.4.6. Concomitant Treatment for Atopic Dermatitis

At each visit (Visit 1-6) dose and type of concomitant treatment will be documented. At baseline visit the number of days with topical-treatment use (TCS, TCI) and emollients use three months before start of treatment with abrocitinib (first visit) and at each subsequent visit number of days with topical- treatment use (TCS, TCI) and emollients use days since the last visit (follow-up visits) will be assessed.

9.2.4.7. Treatment Expectation/Satisfaction

At baseline (Visit 1), the reasons for starting or re-starting therapy with abrocitinib as well as the expectations of this treatment will be gathered from the patient. At subsequent visits (Visits 2-6) the treatment satisfaction with abrocitinib will be requested from the patient.

9.2.4.8. Effectiveness Criteria

The effectiveness of the treatment with abrocitinib will be documented using the following tools for the evaluation of the course of the disease:

Indicator	Definition/Calculation
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).[38]
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.[39]
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

9.2.4.9. Patient-Reported Criteria

The patient-reported criteria will be documented using the following tools for the evaluation of the course of the disease:

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).[40]
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. The maximum POEM score is 28 points.[41]
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 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.[42]
MOS	The Medical Outcomes Study Sleep Scale (MOS-Sleep) includes 12 items assessing sleep disturbance, sleep adequacy, somnolence, quantity of sleep, snoring, and awakening short of breath or with a headache.[43]
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 23 possible treatment goals are evaluated on an importance scale from 0 ("not at all") to 5 ("very").[44,45]
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).[46]

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

9.2.4.10. Safety

All adverse events (AEs) that will occur during the observation period will be documented. For more information, please refer to Section 11. At the final visit or if a patient discontinues with abrocitinib, the healthcare professional (HCP) will be asked to assess the general tolerability of the treatment with abrocitinib and the reasons for discontinuation (intolerability or lack of efficacy) will be analyzed. When applicable severity categories (mild, moderate and severe) of adverse events will be assessed.

9.3. Variables

Table 2. List of Variables

Variable	Role	Data source(s)	Operational definition
AD-treatment with Abrocitinib and/or without topicals – date of initiation	Exposure, Potential confounder, potential subgroup identifier	Case records	Details will be provided in the Statistical Analysis Plan (SAP)
AD-treatment with Abrocitinib and/or without topicals – dose	Exposure, Potential confounder, outcome, potential subgroup identifier	Case records	Details will be provided in SAP
AD-treatment with Abrocitinib and/or without topicals – tolerability/safety	Potential confounder, potential subgroup identifier, safety outcome	Case records	Details will be provided in SAP
Type and results of performed laboratory checks	Potential confounder, potential subgroup identifier, safety outcome	Case records	Details will be provided in SAP
Adverse events	Safety outcome	Case records	Details will be provided in SAP
Age (Year of birth)	Baseline characteristics, potential	Case records	Details will be provided in SAP

Variable	Role	Data source(s)	Operational definition
	confounder, potential subgroup identifier		
Sex	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
Height	Baseline characteristics	Case records	Details will be provided in SAP
Weight	Baseline characteristics	Case records	Details will be provided in SAP
Highest level of education	Baseline characteristics, potential confounder	Case records	Details will be provided in SAP
Ethnicity	Baseline characteristics	Case records	Details will be provided in SAP
Occupational status	Baseline characteristics	Case records	Details will be provided in SAP
Alcohol consumption status	Baseline characteristics, potential confounder	Case records	Details will be provided in SAP
Insurance type	Baseline characteristics	Case records	Details will be provided in SAP
Presence of family history of atopic diseases	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
History of herpes simplex and/or eczema herpeticum and/or herpes zoster	Baseline characteristics	Case records	Details will be provided in SAP
Vaccination status (Herpes zoster, Covid-19, Influenza Varicella)	Baseline characteristics	Case records	Details will be provided in SAP
Age at initial diagnosis of AD	Baseline characteristics, potential confounder	Case records	Details will be provided in SAP

Variable	Role	Data source(s)	Operational definition
Smoking history and current smoking status	Baseline characteristics, potential confounder	Case records	Details will be provided in SAP
Renal and/or liver impairment	Baseline characteristics	Case records	Details will be provided in SAP
Comorbidities of interest (atopic diseases, malignancies, cardiovascular diseases)	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
If positive anamnesis at baseline exists: Improvement of (allergic) asthma symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
If positive anamnesis at baseline exists: Improvement of (allergic) rhinitis symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
If positive anamnesis at baseline exists: Improvement of polyposis nasi symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
If positive anamnesis at baseline exists: Improvement of alopecia areata from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
If positive anamnesis at baseline exists: Improvement of chronic hand eczema symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP

Variable	Role	Data source(s)	Operational definition
If positive anamnesis at baseline exists: Improvement of prurigo nodularis symptoms from baseline	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
Previous treatments for diagnosed AD	Baseline characteristics, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
Number of days with topical-treatment use & number of days with emollients use	Exposure, outcome variable	Case records	Details will be provided in SAP
Concomitant treatment of AD (and dosage)	Baseline characteristics, Exposure, outcome, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
Concomitant (non-AD) treatment	Baseline characteristics, outcome, potential confounder, potential subgroup identifier	Case records	Details will be provided in SAP
Dosage of Abrocitinib used	Exposure, potential confounder, outcome variable, potential subgroup identifier	Case records	Details will be provided in SAP
Compliance with Abrocitinib treatment (patients´ reported compliance)	potential confounder, outcome	Case records	Details will be provided in SAP

Variable	Role	Data source(s)	Operational definition
Reasons for start of Abrocitinib therapy	outcome variable	Case records	Details will be provided in SAP
Reasons for prescribed dose of Abrocitinib therapy	outcome variable	Case records	Details will be provided in SAP
Reasons for discontinuation of Abrocitinib therapy	outcome variable	Case records	Details will be provided in SAP
Number of flares	outcome variable	Case records	Details will be provided in SAP
Number of hospitalizations due to AD	outcome variable	Case records	Details will be provided in SAP
Number of absent days at work/study due to AD	outcome variable	Case records	Details will be provided in SAP
SCORAD	outcome variable	Case records	Details will be provided in SAP
EASI	outcome variable	Case records	Details will be provided in SAP
IGA	outcome variable	Case records	Details will be provided in SAP
Pruritus-NRS	outcome variable	Case records	Details will be provided in SAP
PP- NRS	outcome variable	Case records	Details will be provided in SAP
DLQI	outcome variable	Case records	Details will be provided in SAP
POEM	outcome variable	Case records	Details will be provided in SAP
MOS-Sleep scale	outcome variable	Case records	Details will be provided in SAP
Patient Benefit Index	outcome variable	Case records	Details will be provided in SAP
EQ-5D-5L	outcome variable	Case records	Details will be provided in SAP
HADS	outcome variable	Case records	Details will be provided in SAP

9.4. Data Sources

Patients will be enrolled in a consecutive manner by participating study sites. Site staff will review all necessary information from the patient´s medical record to determine eligibility for enrollment. Patients who fulfill the eligibility criteria will be invited to participate in the non-interventional study. Upon providing written informed consent, patients will be enrolled. The investigator will document patient data collected during routine visits from medical records. All data including the physician´s global assessment of efficacy parameters will be documented in the clinical database (eCRF).

For collection of efficacy and quality parameters assessed from the patient by using patient questionnaires, the patient should fill out the respective questionnaires during the study visit via the tablet PC provided to the study site (see also Section 9.2.3.1). Patients who are unwilling or unable to use the provided tablet PC are allowed to use paper-based questionnaires. Paper-based questionnaires will be checked by the site staff for any personal information. After this review is completed, a copy of the questionnaires will be sent to the CRO which will transcribe the questionnaires into the eCRF. With the patient´s access data, the patient can fill the questionnaires in a web-based manner so that the documented data are directly entered in the patient interface of the eCRF. In this case, the site has to send the filled questionnaires via mail to the delegated CRO in a timely manner so that the documented data can be transferred to the eCRF by qualified and trained personnel. The originals of the filled questionnaires (essential documents) are to be filed in the patient´s medical record by the site staff.

9.5. Study Size

In total, this non-interventional study seeks to enroll at least 750 from approximately 80 study sites across Germany. The patients are planned to be enrolled over a period of 60 months. This observational study aims to obtain real-world data on the patient characteristics, treatment patterns, effectiveness of abrocitinib and patient reported outcomes (PROs) beyond progression, rather than testing any pre-defined hypothesis. In accordance with the non-interventional nature of the study, the analyses will solely be of descriptive and explorative character. Therefore, a formal sample size calculation is not applicable. Furthermore, the large sample size was chosen to support a large range of analyses from overall general scientific questions to specific subgroup questions with sufficient precision. The sample size will ensure that the descriptive data mandated by the primary and secondary endpoints are sufficiently precise and meaningful at subgroup level as well.

9.6. Data Management

As already mentioned in Section 9.2.3.1 and Section 9.4, the data are documented web-based in an eCRF in a pseudonymized manner either by the site personnel or by the patients via tablet PCs (patient questionnaires) or paper-based patient questionnaires provided to the study sites by the sponsor. In case a patient fills out paper-based patient questionnaires, the documented data are transferred to the eCRF by qualified and trained personnel of the delegated CRO.

Edit checks and electronic plausibility checks (ie, triggering of automated queries) will be implemented in the eCRF to notify the user directly during data entry on invalid, missing, unexpectedly unusual or implausible data. Notifications on the latter 2 are implemented to encourage double checking for unusual data entries and ensure high quality data. Notification is done by using warning or error messages, whereby the latter prevents to save the eCRF form until the error is corrected by the user.

In addition to these electronic checks, there are manual checks performed by data management personnel of the delegated CRO. They serve to verify the validity and plausibility of the entered data. These mainly relate to plausibility or cross-checks to verify the correctness and completeness of the data, as well as to protocol deviations and eligibility criteria. In addition, free text entries will be checked on plausibility or any "hidden" information (eg, the existence of a hidden AE/serious adverse event [SAE]) or "prohibited" information (such as a patient's full name or documentation of data after withdrawal of consent). Based on the findings detected during such manual checks, queries will be raised and directly be entered into the eCRF forms by data management personnel and clinical research associates (CRAs). When data have been entered, reviewed and edited, the investigator will be allowed to electronically sign the eCRF according to the agreed project process. Within the eCRF, an audit trail is implemented to be able to trace by whom and when the data was entered or edited. In addition, the set queries and the corresponding answers are also captured and saved in the eCRF.

During web-based data entry, encrypted transmissions are applied for client/server communication via the internet. State of the art encryption technology is used. In addition, the server identifies itself to the client workstation by means of a digital server certificate issued by an authorized certification authority. By this, it is ensured that data are only send to the server of Alcedis GmbH.

Data are protected from potential virtual attacks and physical damage. Furthermore, an encrypted backup onto magnetic tape is performed on a regular basis.

Retrieving data or reports as well as edit or read-only rights are controlled with individual passwords. Access authorization to the eCRF database is individually granted to participating investigators and data entry personnel by means of user accounts.

9.6.1. Case Report Forms (CRFs)/Data Collection Tools (DCTs)/Electronic Data Record

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this NIS.

A CRF is required and should be completed for each included patient. The completed original CRFs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer. The investigator shall ensure that the CRFs are securely stored at the study site in encrypted electronic form and will be password protected to prevent access by unauthorized third parties.

The investigator has ultimate responsibility for the collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms (source documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The CRFs must be signed by the investigator or by an authorized staff member to attest that the data contained on the CRFs are true. Any corrections to entries made in the CRFs or source documents must be dated, initialed, and explained (if necessary) and should not obscure the original entry.

In most cases the source documents are the hospital or the physician's chart. In these cases, data collected on the CRFs must match those charts.

In some cases, the CRF may also serve as the source document. In these cases, a document should be available at the investigator site and at Pfizer that clearly identifies those data that will be recorded on the CRF, and for which the CRF will stand as the source document.

In this non-interventional study, the eCRF serves as source document for the patient questionnaires. The patients can enter the data for the respective questionnaires directly into the tablet, which are then automatically transferred to the eCRF.

9.6.2. Record Retention

To enable evaluations and/or inspections/audits from regulatory authorities or Pfizer, the investigator agrees to keep records, including the identity of all participating patients (sufficient information to link records, eg, CRFs and hospital records), all original signed informed consent documents, copies of all CRFs, safety reporting forms, source documents and essential documents, detailed records of treatment disposition, and adequate documentation of relevant correspondence (eg, letters, meeting minutes, and telephone call reports). The records should be retained by the investigator according to local regulations or as specified in the clinical study agreement (CSA), whichever is longer. The investigator must ensure that the records continue to be stored securely for so long as they are retained.

If the investigator becomes unable for any reason to continue to retain study records for the required period (eg, retirement, relocation), Pfizer should be prospectively notified. The study records must be transferred to a designee acceptable to Pfizer, such as another investigator, another institution, or to an independent third party arranged by Pfizer.

Investigator records must be kept for a minimum of 10 years after completion or discontinuation of the non-interventional study to comply with local German laws.

The investigator must obtain Pfizer's written permission before disposing of any records, even if retention requirements have been met.

9.7. Data Analysis

Due to the nature of the study data, descriptive statistics will be used to summarize all endpoints. No formal hypothesis will be tested.

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in the SAP, which will be dated, filed and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment. Appropriate analysis sets will be defined for statistical analysis.

Time to event endpoints will be investigated using Kaplan-Meier methodology. The time to event will be summarized in terms of medians and 95% confidence interval (CIs). Kaplan-Meier plots of the time to event over the study duration will be presented.

Where appropriate, Cox-Proportional Hazards modelling will be used to assess differences between subgroups.

Definition of time windows for study visits

In order to collect comparable study data, Visits 1 to 3 occurring ±14 days and Visits 3 to 6 occurring ±28 days of the scheduled visit date will be used for data analysis. However, for analysis of safety parameters, all AEs/SAEs documented within the applicable reporting period will be analyzed.

Visit Label	Target Day	Definition [Day window]
Enrollment	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

- 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.

9.8. Quality Control

All study sites will be adequately trained on the principles of the NIS and on the handling of the eCRF prior to enrolling patients. As outlined in Section 9.6, measures involving electronic checks and data management activities will be implemented to reduce documentation of implausible data and enhance data integrity. The delegated CRO will organize on-site and remote monitoring visits by qualified and trained clinical research associates (CRAs) to conduct monitoring visits for progress of the study, performance of the sites and source data verification. All monitoring activities are announced to the sites in advance. If findings are identified that could not be resolved during the monitoring, a follow-up letter is sent to the sites.

9.9. Limitations of the Research Methods

Randomized controlled trials are important and powerful tools in assessing efficacy and safety but have their limitations in terms of generalizability. In order to assess patient characteristics, usage and effectiveness of abrocitinib in a usual care setting, parameters need to be determined by performing observational studies.

Inherent limitations of non-interventional, observational, non-controlled, non-randomized studies are generally the risk of selection/ascertainment bias and usually the lack of a parallel control group, which hampers the interpretation of the causality between treatment and outcomes. Furthermore, as with any "as observed" analysis, there is a potential risk of bias due to missing outcome data; which increases with an increasing number of missing outcome data.

As data captured will be limited to information available from the investigator participating in the NIS under in usual care setting, there is a greater possibility that there will be individual items of missing data (eg, a specific lab value is not documented or a questionnaire not completed). Following up patients, even beyond treatment, discontinuation of abrocitinib and switch to other systemic therapies, should result in a higher proportion of

the patients remaining in the NIS until the planned completion date. Where data are missing, information from the patient at other visits may be used in the primary analysis model to assess predictors of treatment decisions. If the different factors being considered in the primary statistical model to look at impact of treatment change are highly correlated, it may not be clear which of the factors is in fact driving the rate of treatment escalation. Other sensitivity analyses may be explored to assess the impact of any confounding. Further details will be included in the SAP.

Patients selected for study inclusion represent a population who are initiated on abrocitinib as part of a usual care setting. The sample of patients will be obtained from investigators who are willing to participate in the NIS and there is a possibility that certain types of patients will be selected to be prescribed abrocitinib (selection bias) and join the study and this could potentially have an impact on findings of the primary analysis (if the 'type' is expected to impact the rate of treatment escalation). Therefore, study findings may not be generalizable to all AD patients.

9.10. Other Aspects

Not applicable.

10. PROTECTION OF HUMAN SUBJECTS

10.1. Patient Information

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of patient personal data. Such measures will include omitting patient names or other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws.

The personal data will be stored at the study site in encrypted electronic and/or paper form and will be password protected or secured in a locked room to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site shall be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of natural persons with regard to the processing of personal data, when study data are compiled by the site for transfer to Pfizer and other authorized parties, patient names will be removed and will be replaced by a single, specific, numerical code, based on a numbering system defined by Pfizer. All other identifiable data transferred to Pfizer or other authorized parties will be identified by this single, patient-specific code. The investigator site will maintain a confidential list of patients who participated in the NIS, linking each patient's numerical code to his or her actual identity. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of

patients' personal data consistent with the clinical study agreement and applicable privacy laws.

10.2. Patient Consent

The informed consent documents and any patient recruitment materials must be in compliance with local regulatory requirements and legal requirements, including applicable privacy laws.

The informed consent documents used during the informed consent process and any patient recruitment materials must be reviewed and approved by Pfizer, approved by the institutional review board (IRB)/independent ethics committee (IEC) before use, and available for inspection.

The investigator must ensure that each study patient, is fully informed about the nature and objectives of the non-interventional study, the sharing of data relating to the NIS and possible risks associated with participation, including the risks associated with the processing of the patient's personal data. The investigator further must ensure that each study patient is fully informed about his or her right to access and correct his or her personal data and to withdraw consent for the processing of his or her personal data.

The investigator, or a person designated by the investigator, will obtain written informed consent from each patient before any study-specific activity is performed. The investigator will retain the original of each patient's signed consent document.

10.3. Patient Withdrawal

Patients may withdraw from the NIS at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or sponsor for safety, behavioral, or administrative reasons. In any circumstance, every effort should be made to document patient outcome, if applicable. The investigator would inquire about the reason for withdrawal and follow-up with the patient regarding any unresolved adverse events.

If the patient withdraws from the NIS, and also withdraws consent for disclosure of future information, no further evaluations should be performed, and no additional data should be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent, if the patient provides explicit written consent.

Treatment discontinuation does not constitute patient withdrawal. In case of treatment discontinuation, the patient may remain in the study where follow-up documentation can be provided.

10.4. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

It is the responsibility of the investigator to have prospective approval of the non-interventional study protocol, protocol amendments, and informed consent forms, and other relevant documents, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained by the investigator. Copies of IRB/IEC approvals should be forwarded to Pfizer.

10.5. Ethical Conduct of the Study

The NIS will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in §67 (6) of the Medicinal Products Act (AMG, German Drug Law)) and the recommendations for the conduct of non-interventional studies ("Anwendungsbeobachtungen") of the Federal Institute for Drugs and Medical Devices (BfArM) and the Paul-Ehrlich-Institut, recommendations for increasing the quality and transparency of non-interventional studies by the German Association of Research-Based Pharmaceutical Companies (VFA), the Code of Conduct for the Collaboration with Healthcare Professionals by the Voluntary Self-Regulation for the Pharmaceutical Industry (FSA) and the declaration of Helsinki. Furthermore, it will follow generally accepted research practices described in Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE), Good Epidemiological Practice (GEP) guidelines issued by the International Epidemiological Association (IEA), Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), International Ethical Guidelines for Epidemiological Research issued by the Council for International Organizations of Medical Sciences (CIOMS), European Medicines Agency (EMA).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

REQUIREMENTS

The table below summarizes the requirements for recording safety events on the eCRF and for reporting safety events on the non-interventional study (NIS) adverse event monitoring (AEM) Report Form to Pfizer Safety. These requirements are delineated for three types of events: (1) serious adverse events (SAEs); (2) non-serious AEs (as applicable); and (3) scenarios involving drug exposure, including exposure during pregnancy, exposure during breast feeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure. These events are defined in the section "Definitions of Safety Events."

Table 3. Technical Specifications for Safety Reporting.

Safety event	**Recorded on the eCRF**	**Reported via eCRF on the NIS AEM Report Form to Pfizer Safety within 24 hours of awareness**
SAE	All	All
Non-serious AE	All	None
Scenarios involving exposure to a drug under study, including exposure during pregnancy, exposure during breast feeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure	All (regardless of whether associated with an AE), **except occupational exposure**	All (regardless of whether associated with an AE) Note: Any associated AE is reported together with the exposure scenario.

For each AE, the investigator must pursue and obtain information adequate both to determine the outcome of the AE and to assess whether it meets the criteria for classification as a SAE (refer to section "Serious Adverse Events" below).

Safety events according to the far right column of Table 3 above must be reported to Pfizer within 24 hours of awareness of the event by the investigator **regardless of whether the event is determined by the investigator to be related to abrocitinib**. In particular, if the SAE is fatal or life--threatening, notification to Pfizer must be made immediately, irrespective of the extent of available event information. This timeframe also applies to additional new (follow-up) information on previously forwarded safety event reports. In the rare situation that the investigator does not become immediately aware of the occurrence of a safety event, the investigator must report the event within 24 hours after learning of it and document the time of his/her first awareness of the events. In case of technical difficulties or other issues prohibiting the use of the eCRF, only then should the NIS AEM Report Form be used.

For safety events that are considered serious or that are identified in the far right column of the table above that are reportable to Pfizer within 24 hours of awareness, the investigator is obligated to pursue and to provide any additional information to Pfizer in accordance with this 24-hour timeframe. In addition, an investigator may be requested by Pfizer to obtain specific follow-up information in an expedited fashion. This information is more detailed than that recorded on the eCRF. In general, this will include a description of the AE in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a patient death, a

summary of available autopsy findings must be submitted as soon as possible to Pfizer or its designated representative.

Reporting period

For each patient, the safety event reporting period begins at the time of the patient's informed consent, which is obtained prior to the patient's enrollment in the study and lasts through the end of the observation period of the study; a report must be submitted to Pfizer Safety (or its designated representative) for any of the types of safety events listed in the table above occurring during this period. Most often, the date of informed consent is the same as the date of enrollment. In some situations, there may be a lag between the dates of informed consent and enrollment. In these instances, if a patient provides informed consent but is never enrolled in the study (eg, patient changes his/her mind about participation), the reporting period ends on the date of the decision to not enroll the patient. If the investigator becomes aware of a SAE occurring at any time after completion of the study and s/he considers the serious AE to be related to a Pfizer product, the SAE also must be reported to Pfizer Safety.

Causality assessment

The investigator is required to assess and record the causal relationship. For all AEs, sufficient information should be obtained by the investigator to determine the causality of each AE. For AEs with a causal relationship to abrocitinib, follow-up by the investigator is required until the event and/or its sequelae resolve or stabilize at a level acceptable to the investigator, and Pfizer concurs with that assessment.

An investigator's causality assessment is the determination of whether there exists a reasonable possibility that abrocitinib caused or contributed to an AE. If the investigator's final determination of causality is "unknown" and s/he cannot determine whether abrocitinib caused the event, the safety event must be reported within 24 hours.

If the investigator cannot determine the etiology of the event but s/he determines that abrocitinib did not cause the event, this should be clearly documented on the eCRF and in case of technical difficulties only, this also applies to the NIS AEM Report Form.

DEFINITIONS OF SAFETY EVENTS

Adverse events

An AE is any untoward medical occurrence in a patient administered a medicinal product. The event need not necessarily have a causal relationship with the product treatment or usage. Examples of AEs include but are not limited to:

- Abnormal test findings (see below for circumstances in which an abnormal test finding constitutes an AE);

- Clinically significant signs and symptoms;
- Changes in physical examination findings;
- Hypersensitivity;
- Progression/worsening of underlying disease;
- Lack of efficacy;
- Drug abuse;
- Drug dependency.

Additionally, for medicinal products, they may include the signs or symptoms resulting from:

- Drug overdose;
- Drug withdrawal;
- Drug misuse;
- Off-label use;
- Drug interactions;
- Extravasation;
- Exposure during pregnancy;
- Exposure during breast feeding;
- Medication error;
- Occupational exposure.

Abnormal test findings

The criteria for determining whether an abnormal objective test finding should be reported as an AE are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or

- Test result leads to a change in study dosing or discontinuation from the NIS, significant additional concomitant drug treatment, or other therapy; and/or

- Test result is considered to be an AE by the investigator or sponsor.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an AE. Any abnormal test result that is determined to be an error does not require reporting as an AE.

Serious adverse events

A SAE is any untoward medical occurrence in a patient administered a medicinal or nutritional product (including pediatric formulas) at any dose that:

- Results in death;

- Is life-threatening;

- Requires inpatient hospitalization or prolongation of hospitalization (see below for circumstances that do not constitute AEs);

- Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);

- Results in congenital anomaly/birth defect.

Medical and scientific judgment is exercised in determining whether an event is an important medical event. An important medical event may not be immediately life-threatening and/or result in death or hospitalization. However, if it is determined that the event may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above, the important medical event should be reported as serious.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse.

Additionally, any suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic, is considered serious. The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a patient exposed to a Pfizer product. The terms “suspected transmission” and “transmission” are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance (PV) personnel. Such cases are also considered for reporting as product defects, if appropriate.

Hospitalization

Hospitalization is defined as any initial admission (even if less than 24 hours) to a hospital or equivalent healthcare facility or any prolongation to an existing admission. Admission also includes transfer within the hospital to an acute/intensive care unit (eg, from the psychiatric wing to a medical floor, medical floor to a coronary care unit, neurological floor to a tuberculosis unit). An emergency room visit does not necessarily constitute a hospitalization; however, an event leading to an emergency room visit should be assessed for medical importance.

Hospitalization in the absence of a medical AE is not in itself an AE and is not reportable. For example, the following reports of hospitalization without a medical AE are not to be reported.

- Social admission (eg, patient has no place to sleep)
- Administrative admission (eg, for yearly exam)
- Optional admission not associated with a precipitating medical AE (eg, for elective cosmetic surgery)
- Hospitalization for observation without a medical AE
- Admission for treatment of a pre-existing condition not associated with the development of a new AE or with a worsening of the pre-existing condition (eg, for work-up of persistent pre-treatment lab abnormality).

Scenarios necessitating reporting to Pfizer Safety within 24 hours

Scenarios involving exposure during pregnancy, exposure during breastfeeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure are described below.

Exposure during pregnancy

An exposure during pregnancy (EDP) occurs if:

1. A female becomes, or is found to be, pregnant either while receiving or having been exposed to (eg, environmental) abrocitinib, or the female becomes, or is found to be, pregnant after discontinuing and/or being exposed to abrocitinib (maternal exposure).

An example of environmental exposure would be a case involving direct contact with a Pfizer product in a pregnant woman (eg, a nurse reports that she is pregnant and has been exposed to chemotherapeutic products).

2. A male has been exposed, either due to treatment or environmental exposure to abrocitinib prior to or around the time of conception and/or is exposed during the partner pregnancy (paternal exposure).

For exposure during pregnancy in studies of pregnant women, data on the exposure to abrocitinib during pregnancy, are not reportable unless associated with serious or non-serious adverse events.

As a general rule, prospective and retrospective exposure during pregnancy reports from any source are reportable irrespective of the presence of an associated AE and the procedures for SAE reporting should be followed, with the exception of those studies conducted in pregnant women (as described in above), for which data on the exposure are not reportable unless associated with serious or non-serious adverse events.

If a study participant or study participant's partner becomes, or is found to be, pregnant during the study participant's treatment with abrocitinib, this information must be submitted to Pfizer, irrespective of whether an AE has occurred using theNIS AEM Report Form and the EDP Supplemental Form (please refer to Annex 1). In addition, the information regarding environmental exposure to abrocitinib in a pregnant woman (eg, a patient reports that she is pregnant and has been exposed to a cytotoxic product by inhalation or spillage) must be submitted using the NIS AEM Report Form and the EDP Supplemental Form. The EDP Supplemental Form must not be submitted if consent by the pregnant person is not given and documented. This must be done irrespective of whether an AE has occurred.

Information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

Follow-up is conducted to obtain general information on the pregnancy; in addition, follow-up is conducted to obtain information on EDP outcome for all EDP reports with pregnancy outcome unknown. A pregnancy is followed until completion or until pregnancy termination (eg, induced abortion) and Pfizer is notified of the outcome. This information is provided as a follow-up to the initial EDP report. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless preprocedure-test findings are conclusive for a congenital anomaly and the findings are reported).

If the outcome of the pregnancy meets the criteria for an SAE (eg, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly [in a live born, a terminated fetus, an intrauterine fetal demise, or a neonatal death]), the procedures for reporting SAEs should be followed.

Additional information about pregnancy outcomes that are reported as SAEs follows:

- Spontaneous abortion includes miscarriage and missed abortion;
- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to investigational product.

Additional information regarding the exposure during pregnancy may be requested. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays).

In the case of paternal exposure, the study participant will be provided with the Pregnant Partner Release of Information Form to deliver to his partner. It must be documented that the study participant was given this letter to provide to his partner.

Exposure during breastfeeding

Scenarios of exposure during breastfeeding must be reported, irrespective of the presence of an associated AE. An exposure during breastfeeding report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accord with authorized use. However, if the infant experiences an AE associated with such a drug's administration, the AE is reported together with the exposure during breastfeeding.

Medication error

A medication error is any unintentional error in the prescribing, dispensing, or administration of a medicinal product that may cause or lead to inappropriate medication use or patient harm while in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems including: prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Medication errors include:

- Near misses, involving or not involving a patient directly (eg, inadvertent/erroneous administration, which is the accidental use of a product outside of labeling or prescription on the part of the healthcare provider or the patient/consumer);
- Confusion with regard to invented name (eg, trade name, brand name).

The investigator must submit the following medication errors to Pfizer, irrespective of the presence of an associated AE/SAE:

- Medication errors involving patient exposure to the product, whether or not the medication error is accompanied by an AE.
- Medication errors that do not involve a patient directly (eg, potential medication errors or near misses). When a medication error does not involve patient exposure to the product the following minimum criteria constitute a medication error report:
- An identifiable reporter;
- A suspect product;
- The event medication error.

Overdose, Misuse, Extravasation

Reports of overdose, misuse, and extravasation associated with the use of a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE.

Lack of Efficacy

- Reports of lack of efficacy to a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE or the indication for use of the Pfizer product.

Occupational Exposure

- Reports of occupational exposure to a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE.

11.1. Single Reference Safety Document

The respective current local product label ("Fachinformation Germany") will serve as the single reference safety document during the course of the non-interventional study, which will be used by Pfizer safety to assess any safety events reported to Pfizer Safety by the investigator during the course of this NIS. The single reference safety document should be used by the investigator for prescribing purposes and guidance.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

In the event of any prohibition or restriction imposed (eg, clinical hold) by an applicable competent authority in any area of the world, or if the investigator is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study patients against any immediate hazard, and of any serious breaches of this NI study protocol that the investigator becomes aware of.

13. REFERENCES

1. Barbarot S, Auziere S, Gadkari A, Girolomoni G, Puig L, Simpson EL, et al. Epidemiology of atopic dermatitis in adults: Results from an international survey. Allergy. 2018;73(6):1284-93. Epub 20180213. doi: 10.1111/all.13401. PubMed PMID: 29319189.

2. Schmitz R, Atzpodien K, Schlaud M. Prevalence and risk factors of atopic diseases in German children and adolescents. Pediatr Allergy Immunol. 2012;23(8):716-23. Epub 20120813. doi: 10.1111/j.1399-3038.2012.01342.x. PubMed PMID: 22882467.

3. Kim JP, Chao LX, Simpson EL, Silverberg JI. Persistence of atopic dermatitis (AD): A systematic review and meta-analysis. J Am Acad Dermatol. 2016;75(4):681-7 e11. Epub 20160817. doi: 10.1016/j.jaad.2016.05.028. PubMed PMID: 27544489; PubMed Central PMCID: PMC5216177.

4. Ring J, Zink A, Arents BWM, Seitz IA, Mensing U, Schielein MC, et al. Atopic eczema: burden of disease and individual suffering - results from a large EU study in adults. J Eur Acad Dermatol Venereol. 2019;33(7):1331-40. Epub 20190606. doi: 10.1111/jdv.15634. PubMed PMID: 31002197.

5. Darsow U, Pfab F, Valet M, Tolle TR, Ring J. Itch and eczema. Chem Immunol Allergy. 2012;96:81-8. Epub 20120313. doi: 10.1159/000331890. PubMed PMID: 22433375.

6. Williams HC. Clinical practice. Atopic dermatitis. N Engl J Med. 2005;352(22):2314-24. doi: 10.1056/NEJMcp042803. PubMed PMID: 15930422.

7. Werfel T, Heratizadeh A, Aberer W, Ahrens F, Augustin M, Biedermann T, et al. Aktualisierung „Systemtherapie bei Neurodermitis“ zur S2k-Leitlinie Neurodermitis. J Dtsch Dermatol Ges. 2021;19(1):151-69. doi: 10.1111/ddg.14371_g. PubMed PMID: 33491881.

8. Leung DY, Bieber T. Atopic dermatitis. Lancet. 2003;361(9352):151-60. doi: 10.1016/S0140-6736(03)12193-9. PubMed PMID: 12531593.

9. Ring J, Alomar A, Bieber T, Deleuran M, Fink-Wagner A, Gelmetti C, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) part I. J Eur Acad Dermatol Venereol. 2012;26(8):1045-60. doi: 10.1111/j.1468-3083.2012.04635.x. PubMed PMID: 22805051.

10. Gooderham MJ, Hong HC, Eshtiaghi P, Papp KA. Dupilumab: A review of its use in the treatment of atopic dermatitis. J Am Acad Dermatol. 2018;78(3 Suppl 1):S28-S36. doi: 10.1016/j.jaad.2017.12.022. PubMed PMID: 29471919.

11. Sanofi. Dupixent: EPAR - Product Information. European Medicines Agency; 2023.

12. Tsoi LC, Rodriguez E, Degenhardt F, Baurecht H, Wehkamp U, Volks N, et al. Atopic Dermatitis Is an IL-13-Dominant Disease with Greater Molecular Heterogeneity Compared to Psoriasis. J Invest Dermatol. 2019;139(7):1480-9. Epub 20190111. doi: 10.1016/j.jid.2018.12.018. PubMed PMID: 30641038; PubMed Central PMCID: PMC6711380.

13. Wollenberg A, Blauvelt A, Guttman-Yassky E, Worm M, Lynde C, Lacour JP, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol. 2021;184(3):437-49. Epub 20201230. doi: 10.1111/bjd.19574. PubMed PMID: 33000465; PubMed Central PMCID: PMC7986411.

14. Pharma L. Adtralza : EPAR - Product Information. European Medicines Agency2022.

15. Lilly E. Olumiant : EPAR - Product Information. European Medicines Agency2023.

16. AbbVie. Rinvoq : EPAR - Product Information. European Medicines Agency2023.

17. Blauvelt A, de Bruin-Weller M, Gooderham M, Cather JC, Weisman J, Pariser D, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet. 2017;389(10086):2287-303. Epub 20170504. doi: 10.1016/S0140-6736(17)31191-1. PubMed PMID: 28478972.

18. Simpson EL, Sinclair R, Forman S, Wollenberg A, Aschoff R, Cork M, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet. 2020;396(10246):255-66. doi: 10.1016/S0140-6736(20)30732-7. PubMed PMID: 32711801.

19. Silverberg JI, Simpson EL, Thyssen JP, Gooderham M, Chan G, Feeney C, et al. Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol. 2020;156(8):863-73. doi: 10.1001/jamadermatol.2020.1406. PubMed PMID: 32492087; PubMed Central PMCID: PMC7271424.

20. Halling-Overgaard AS, Zachariae C, Thyssen JP. Management of Atopic Hand Dermatitis. Dermatol Clin. 2017;35(3):365-72. doi: 10.1016/j.det.2017.02.010. PubMed PMID: 28577805.

21. Agner T, Elsner P. Hand eczema: epidemiology, prognosis and prevention. J Eur Acad Dermatol Venereol. 2020;34 Suppl 1:4-12. doi: 10.1111/jdv.16061. PubMed PMID: 31860734.

22. Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. Lancet. 2020;396(10247):345-60. doi: 10.1016/S0140-6736(20)31286-1. PubMed PMID: 32738956.

23. Elsner P, Agner T. Hand eczema: treatment. J Eur Acad Dermatol Venereol. 2020;34 Suppl 1:13-21. doi: 10.1111/jdv.16062. PubMed PMID: 31860736.

24. Cheng J, Facheris P, Ungar B, Guttman-Yassky E. Current emerging and investigational drugs for the treatment of chronic hand eczema. Expert Opin Investig Drugs. 2022;31(8):843-53. Epub 20220617. doi: 10.1080/13543784.2022.2087059. PubMed PMID: 35658708.

25. Davis DMR, Drucker AM, Alikhan A, Bercovitch L, Cohen DE, Darr JM, et al. American Academy of Dermatology Guidelines: Awareness of comorbidities associated with atopic dermatitis in adults. J Am Acad Dermatol. 2022;86(6):1335-6 e18. Epub 20220124. doi: 10.1016/j.jaad.2022.01.009. PubMed PMID: 35085682.

26. Wenzel S, Castro M, Corren J, Maspero J, Wang L, Zhang B, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting beta2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. Lancet. 2016;388(10039):31-44. Epub 20160427. doi: 10.1016/S0140-6736(16)30307-5. PubMed PMID: 27130691.

27. Castro M, Corren J, Pavord ID, Maspero J, Wenzel S, Rabe KF, et al. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. N Engl J Med. 2018;378(26):2486-96. Epub 20180521. doi: 10.1056/NEJMoa1804092. PubMed PMID: 29782217.

28. Laidlaw TM, Bachert C, Amin N, Desrosiers M, Hellings PW, Mullol J, et al. Dupilumab improves upper and lower airway disease control in chronic rhinosinusitis with nasal polyps and asthma. Ann Allergy Asthma Immunol. 2021;126(5):584-92 e1. Epub 20210116. doi: 10.1016/j.anai.2021.01.012. PubMed PMID: 33465455.

29. King B, Ohyama M, Kwon O, Zlotogorski A, Ko J, Mesinkovska NA, et al. Two Phase 3 Trials of Baricitinib for Alopecia Areata. N Engl J Med. 2022;386(18):1687-99. Epub 20220326. doi: 10.1056/NEJMoa2110343. PubMed PMID: 35334197.

30. King B, Zhang X, Harcha WG, Szepietowski JC, Shapiro J, Lynde C, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b-3 trial. Lancet. 2023;401(10387):1518-29. Epub 20230414. doi: 10.1016/S0140-6736(23)00222-2. PubMed PMID: 37062298.

31. Agency EM. Olumiant: EPAR - Procedural steps taken and scientific information after authorisation. 2023.

32. Zeidler C, Yosipovitch G, Stander S. Prurigo Nodularis and Its Management. Dermatol Clin. 2018;36(3):189-97. Epub 20180320. doi: 10.1016/j.det.2018.02.003. PubMed PMID: 29929592.

33. Stander S, Yosipovitch G, Legat FJ, Lacour JP, Paul C, Narbutt J, et al. Trial of Nemolizumab in Moderate-to-Severe Prurigo Nodularis. N Engl J Med. 2020;382(8):706-16. doi: 10.1056/NEJMoa1908316. PubMed PMID: 32074418.

34. Furue M, Furue M. Interleukin-31 and Pruritic Skin. J Clin Med. 2021;10(9). Epub 20210428. doi: 10.3390/jcm10091906. PubMed PMID: 33924978; PubMed Central PMCID: PMC8124688.

35. Huang AH, Williams KA, Kwatra SG. Prurigo nodularis: Epidemiology and clinical features. J Am Acad Dermatol. 2020;83(6):1559-65. Epub 20200523. doi: 10.1016/j.jaad.2020.04.183. PubMed PMID: 32454098.

36. Paller A, Jaworski JC, Simpson EL, Boguniewicz M, Russell JJ, Block JK, et al. Major Comorbidities of Atopic Dermatitis: Beyond Allergic Disorders. Am J Clin Dermatol. 2018;19(6):821-38. doi: 10.1007/s40257-018-0383-4. PubMed PMID: 30168085.

37. Pratt CH, King LE, Jr., Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nat Rev Dis Primers. 2017;3:17011. Epub 20170316. doi: 10.1038/nrdp.2017.11. PubMed PMID: 28300084; PubMed Central PMCID: PMC5573125.

38. Kunz B, Oranje AP, Labreze L, Stalder JF, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. Dermatology. 1997;195(1):10-9. doi: 10.1159/000245677. PubMed PMID: 9267730.

39. Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. Exp Dermatol. 2001;10(1):11-8. doi: 10.1034/j.1600-0625.2001.100102.x. PubMed PMID: 11168575.

40. Yosipovitch G, Reaney M, Mastey V, Eckert L, Abbe A, Nelson L, et al. Peak Pruritus Numerical Rating Scale: psychometric validation and responder definition for assessing itch in moderate-to-severe atopic dermatitis. Br J Dermatol. 2019;181(4):761-9. Epub 20190501. doi: 10.1111/bjd.17744. PubMed PMID: 30729499; PubMed Central PMCID: PMC6850643.

41. Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. Arch Dermatol. 2004;140(12):1513-9. doi: 10.1001/archderm.140.12.1513. PubMed PMID: 15611432.

42. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19(3):210-6. doi: 10.1111/j.1365-2230.1994.tb01167.x. PubMed PMID: 8033378.

43. Hays RD, Stewart AL. Sleep measures. In: Stewart AL, Ware JE, editors. Measuring Functioning and Well-being: The Medical Outcomes Study Approach: Duke University Press; 1992. p. 235-59.

44. Augustin M, Radtke MA, Zschocke I, Blome C, Behechtnejad J, Schafer I, et al. The patient benefit index: a novel approach in patient-defined outcomes measurement for skin diseases. Arch Dermatol Res. 2009;301(8):561-71. Epub 20090327. doi: 10.1007/s00403-009-0928-8. PubMed PMID: 19326133.

45. Blome C, Augustin M, Behechtnejad J, Rustenbach SJ. Dimensions of patient needs in dermatology: subscales of the patient benefit index. Arch Dermatol Res. 2011;303(1):11-7. Epub 20100817. doi: 10.1007/s00403-010-1073-0. PubMed PMID.

46. Greiner W, Weijnen T, Nieuwenhuizen M, Oppe S, Badia X, Busschbach J, et al. A single European currency for EQ-5D health states. Results from a six-country study. Eur J Health Econ. 2003;4(3):222-31. doi: 10.1007/s10198-003-0182-5. PubMed PMID: 15609189.

14. LIST OF TABLES

15. LIST OF FIGURES

ANNEX 1. LIST OF STAND ALONE DOCUMENTS

Number	Document reference number	Date	Title
1	Section 11	16JUN2023	B7451089_Pregnancy Reporting Process_V1_16JUN2023

ANNEX 2. ADDITIONAL INFORMATION

Not applicable.