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STUDY PROTOCOL

PsABIOnd Study and eDaily Substudy Design: Long-Term Effectiveness and Safety of Guselkumab and IL-17 Inhibitors in Routine Clinical Practice in Patients with Psoriatic Arthritis

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ABSTRACT

Introduction: Randomised clinical studies in psoriatic arthritis (PsA) do not always reflect patients in routine clinical practice. Large-scale data from routine practice are needed to better understand drug persistence, effectiveness and long-term safety of therapeutic agents.

Methods: PsABIOnd is an international, prospective, observational study designed to collect long-term routine care data in patients with PsA who receive guselkumab (an interleukin-23 [IL-23] inhibitor) or an interleukin-17 (IL-17) inhibitor. Adult patients (≥ 18 years) with a confirmed diagnosis of PsA who are starting guselkumab or any approved IL-17 inhibitor as a first, second, third or fourth line of PsA treatment and who provide written informed consent will be eligible to participate. Participants will be followed for a maximum of 36 months (+3 months) from the start of treat-

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ment. Study visits will occur in line with the standard of care, approximately every 6 months, plus an additional visit at 3 months after the start of treatment. eDaily by PsABIOnd - aneHealth substudy, will document the impact of these treatments on wellbeing and symptoms in a subgroup of participants over a 24-week (+4 weeks) observation period on treatment.

Planned Outcomes: The primary objective of PsABIOnd is to evaluate treatment persistence with guselkumab and IL-17 inhibitors. Data sources will include validated electronic patient-reported outcomes (ePROs) and physician-completed assessments. Safety data will be collected through reporting adverse events. The eDaily by PsABIOnd substudy will use wearable and digital technologies for continuous activity and sleep monitoring, and frequent patient eDiary and ePRO collection to provide a more detailed and comprehensive picture of PsA.

Trial Registration: ClinicalTrials.gov identifier: NCT05049798.

PLAIN LANGUAGE SUMMARY

Psoriatic arthritis (PsA) is a type of arthritis associated with inflammation that occurs in almost one-third of patients with the inflammatory skin condition psoriasis. PsA can vary between individuals, and typically causes joint pain, swelling and stiffness, affecting both physical and social well-being. Over the past decade, several new PsA treatments have become available. However, there is currently a lack of agreement about the best treatment options. As PsA is a chronic (long-term) disease, the duration of time a patient continues taking a prescribed treatment (termed "treatment persistence") is important. The randomised clinical trials used to determine if a treatment works use strict rules to select patients. Therefore, large studies from everyday practice are needed to better understand the effectiveness and safety of these PsA treatments for a wider range of patients. PsABIOnd is a real-life study that will compare guselkumab (an interleukin-23 inhibitor) and interleukin-17 inhibitors, which are two relatively new types of PsA treatments. The study will provide information about how long patients remain on these treatments and how effectively and safely they work over a 3-year period. PsABIOnd will also explore the impact of PsA on participants' lives by collecting information about their quality of life, disease activity and treatment satisfaction. In addition, participants also taking part in the eDaily by PsABIOnd substudy will wear a watch-like device and use a smartphone-based app to record measurements including activity, sleep, pain and well-being to give a detailed picture of PsA and its impact on patients' daily lives.

Keywords: Psoriatic arthritis; Real-world evidence; Guselkumab; Biological disease-modifying anti-rheumatic drugs (bDMARDs); IL-17 inhibitors; eHealth

Key Summary Points

Randomised clinical studies in psoriatic arthritis (PsA) do not always reflect patients in routine clinical practice.

PsABIOnd is an observational prospective study of patients with PsA receiving guselkumab and interleukin-17 inhibitors that will provide long-term data on the persistence, effectiveness and safety of these therapies in routine practice.

PsABIOnd will also explore the impact of PsA from the patients' perspective by collecting electronic patient-reported outcomes (ePROs).

The eDaily by PsABIOnd substudy will use continuous activity and sleep monitoring and frequent patient diary and ePRO collection to provide a more detailed and comprehensive clinical picture of PsA.

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INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease associated with psoriasis with an estimated worldwide prevalence rate of 133 cases per 100,000 population [1, 2]. PsA is characterised by a complex and heterogeneous clinical presentation that can span multiple domains of axial and/or peripheral arthritis, dactylitis, enthesitis, and psoriasis of skin or nails, and can impair physical and social functioning [2, 3]. PsA is also associated with extra-articular manifestations, for example inflammatory bowel disease, and multimorbidity, exemplified by obesity, cardiometabolic disease, depression and anxiety [4].

The last decade has seen several effective treatment options become available to treat patients with PsA. However, the increasing number of therapies has led to increased complexity in treatment guidelines and resulted in a lack of consensus across recommendations issued by the American College of Rheumatology (ACR), the European Alliance of Associations for Rheumatology (EULAR) and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) [3, 5–8]. The lack of consensus can partially be explained by different methods used for recommendation development and a slightly different focus of the research groups. Furthermore, there is evidence suggesting that the results of clinical studies – the main data source used for developing treatment guidelines – may not be directly transferable to routine clinical practice [9].

Randomised clinical trials (RCTs), the gold standard of clinical treatment research, are limited by stringent selection criteria, with prespecified disease activity levels and limited comorbidities, and consequently provide safety and efficacy data in a selected patient population. Several studies have shown that only a small minority of patients in routine clinical practice with PsA, rheumatoid arthritis (RA) or psoriasis would qualify for participation in RCTs, highlighting some of the limitations of using RCTs as the only source of data to inform guidelines and clinical practice [10–15]. Treatment efficacy, measured under ideal conditions in RCTs, may not be fully aligned with real-world treatment effectiveness. It has been suggested that treatment persistence in routine care, reflecting a combination of effectiveness, tolerability and safety, is a better reflection of overall effectiveness than responses measured in RCTs [16]. As a chronic disease, treatment persistence in PsA should be a key element of clinical care. As such, data from large-scale routine practice are needed to better understand persistence and effectiveness as well as to provide long-term information on the safety of therapeutic agents, particularly those that have reached the clinic more recently and where clinical experience is thus more limited. One large-scale, real-world study [the Norwegian disease-modifying antirheumatic drug (NOR-DMARD) study] has previously shown that patients with an inadequate response to a first tumour necrosis factor (TNF) inhibitor subsequently had poorer responses and lower treatment persistence when switched to a second TNF inhibitor, highlighting the need for a treatment with an alternative mechanism of action in patients who do not respond to their initial biologic treatment [17].

The PsABIOnd prospective, observational study is designed to collect long-term routine care data in patients with PsA who receive guselkumab [an interleukin-23 (IL-23) inhibitor] or an interleukin-17 (IL-17) inhibitor as either first biologic or switching from other biological disease-modifying anti-rheumatic drugs (bDMARDs) or Janus kinase (JAK) inhibitors. This will be a worldwide study with the participation of 20 countries. To understand the value of interventions, it is also important to determine how PsA and therapies used to treat PsA impact on patients. Therefore, PsABIOnd will also explore the impact of PsA from the patients' perspective by collecting electronic patient-reported outcomes (ePROs). Furthermore, eDaily by PsABIOnd—an eHealth substudy, will capture data more frequently than in standard clinical practice via continuous activity, sleep monitoring and daily assessments using a wearable actigraphy device and smartphone-based app to give the most detailed picture of PsA and its impact on patients' daily life.

METHODS

Study Design

PsABIOnd (ClinicalTrials.gov identifier: NCT05049798) is a prospective, observational cohort study across 20 countries (Argentina, Australia, Austria, Belgium, Brazil, Canada, Colombia, France, Germany, Greece, Italy, Japan, Mexico, the Netherlands, South Korea, Spain, Sweden, Switzerland, Taiwan and the United Kingdom) that will collect data on adult patients with a confirmed diagnosis of PsA who are starting guselkumab or an IL-17 inhibitor as a first, second, third or fourth line of PsA biologic therapy per standard clinical practice and licence. Study treatments (index drugs) include guselkumab and IL-17 inhibitor therapies. Non-index drugs are all other bDMARDs, including TNF inhibitors, other IL-23 inhibitors and JAK inhibitors. Index drugs and non-index drugs count as separate lines of biological treatment both before and during the study.

All aspects of treatment and clinical management of participants in this observational study will follow routine clinical practice or any local and overarching guidelines, and all treatment decisions will be at the sole discretion of the treating rheumatologist prior to, and independently of, participation in the study. The study plans to enrol up to approximately 1300 participants, including approximately 650 patients who start receiving guselkumab and approximately 650 patients who start receiving an IL-17 inhibitor at study entry. To minimise the chance of unequal distribution between cohorts, enrolment will be reviewed at least every 6 months, and participating rheumatology centres will pause enrolment in the over-represented cohort while continuing enrolment in the other cohort until distribution is balanced between cohorts.

Study Objectives

The primary objective of this study is to evaluate the treatment persistence with guselkumab and IL-17 inhibitors initiated at enrolment into PsABIOnd (Table 1).

The secondary objectives are to evaluate effectiveness in terms of validated musculoskeletal and composite outcomes of index treatments, to examine potential predictors of response, to describe treatment persistence and treatment patterns for different lines of biological treatment, to collect safety data, to investigate presence and clinical features of concomitant conditions (e.g. psoriasis, uveitis) and comorbidities (e.g. cardiovascular disease), to evaluate the disease and treatment effectiveness from the patient perspective [quality of life (QoL), disease impact, work productivity, etc.], to identify and assess predictors of treatment persistence, and to explore reasons for stopping/switching treatments for PsA (Table 1).

Participant Selection (Main Study)

Adult patients (aged 18 years or older) will be eligible to participate in the study if they have a confirmed diagnosis of PsA determined by a rheumatologist with reference to ClASsification criteria for Psoriatic ARthritis (CASPAR) [18], and start guselkumab or any approved IL-17 inhibitor as a first, second, third or fourth line of bDMARD therapy for PsA as part of their routine clinical care. All participants will be required to provide written informed consent, confirming study participation and allowing for data collection and source verification, before any study-related procedures. Patients will not be eligible to take part in the study if they start guselkumab or an IL-17 inhibitor as fifth or further line of bDMARD, have already received guselkumab or the specific IL-17 inhibitor index treatment, have previously received an investigational drug or used an investigational device within 30 days of study start, are currently enrolled in an interventional study or Janssen-sponsored observational study, or are unwilling or unable to participate in long-term data collection. For the purpose of this study, a switch from a branded originator bDMARD to related biosimilar(s) or vice versa will not be considered a separate treatment line, i.e. will be counted as one prior line of bDMARD therapy.

All participants who provide their written consent for data collection and receive at least

Table 1 Study objectives and measurements

Objective	Objective-related measurements
Primary objective	
To evaluate treatment persistence with guselkumab and IL-17 inhibitor initiated at enrolment into PsABIOnd	The start and stop date (first and last administration dates) of guselkumab and index IL-17 inhibitor treatments will be recorded for each participant
Secondary objectives	
To evaluate effectiveness parameters	Baseline demographics and change from baseline in the following:
	Joint counts (66 joint count for swelling and 68 joint count for tenderness)
	PGA-PsA
	Dactylitis digit count (number of affected digits, 0–20)
	LEI score (enthesitis assessment)
	Presence of nail involvement and number of affected nails (0–20)
	BSA
	CRP
	MDA/VLDA
	cDAPSA/DAPSA
	ePROs[a]
To examine potential predictors of response	Response: defined as a clinical improvement in cDAPSA/DAPSA
To describe treatment persistence and treatment patterns for different lines of biologic treatments	The start and stop date (first and last administration dates) of guselkumab and index IL-17 inhibitor treatments and the sequence of treatment lines
To collect safety-related data in patients with PsA	All adverse events
To investigate presence and clinical features of concomitant disease (e.g. psoriasis, uveitis) and comorbidities (e.g. cardiovascular disease, metabolic syndrome, inflammatory bowel disease and anxiety/depression)	Adverse event data
	BSA psoriasis skin involvement
	Rheumatic disease comorbidity index

Table 1 continued

Objective	Objective-related measurements
To evaluate the disease and drug effectiveness from the patients' perspective (ePROs), including quality of life, disease impact, productivity, health economic outcomes and patient treatment satisfaction	Evaluation of ePRO at baseline, change from baseline and other related endpoints: FiRST EQ-5D-5L HAQ-DI PsAID-12 Pain and patient global VAS scores BASDAI and derived ASDAS-CRP DLQI PASS WPAI:PsA TSQM-9
To identify and assess predictors of treatment persistence	All assessments
To explore detailed reasons for stopping/switching particular PsA treatment during the study	Endpoints related to switching or stopping treatment (i.e. reasons for discontinuation)

ASDAS Ankylosing Spondylitis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BSA* body surface area, *(c)DAPSA* (clinical) Disease Activity Index for Psoriatic Arthritis, *CRP* C-reactive protein, *DLQI* Dermatology Life Quality Index, *ePRO* electronic patient-reported outcome, *EQ 5D 5L* EuroQoL 5 Dimension, 5-Level, *FiRST* Fibromyalgia Rapid Screening Tool, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *IL-17* interleukin 17, *LEI* Leeds Enthesitis Index, *MDA* minimal disease activity, *PASS* patient acceptable symptom state, *PGA* Rheumatologist's Global Assessment of Disease Activity, *PsA* psoriatic arthritis, *PsAID-12* Psoriatic Arthritis Impact of Disease-12, *TSQM* Treatment Satisfaction Questionnaire for Medication, *VAS* visual analogue scale, *VLDA* very low disease activity, *WPAI* Work Productivity and Activity Impairment Questionnaire

[a]See Table 2 for a full list of ePROs

one dose of an index drug during the study will be included in the analyses.

Study Visit Schedule

After a treatment decision has been taken by the treating rheumatologist, eligible patients will be enrolled in the study, and baseline data will be recorded.

Participants will be followed for a maximum of 36 months (+3 months) from the first administration of the initial index treatment. The treatment period will begin on the day the participant receives the first administration of index treatment, and all subsequent visits will be calculated according to this date, except when a switch in bDMARD or switch to a JAK inhibitor treatment takes place. Treatment interruptions of less than 3 months (93 days) will be considered a 'drug holiday' and will not be considered as stopping treatment. Study visits (data collection time points) will occur in line with the standard of care and are expected to happen every 6 (±3) months, plus an additional visit at 3 months after the participant's first dose of their initial index treatment with guselkumab or an IL-17 inhibitor (Fig. 1A).

Table 2 Data collection schedule (main study)

Assessment	Baseline	Study visit[a]
Patient information		
Informed consent	✔	–
Record of patient selection criteria	✔	–
Demographic information		
Gender, age, height	✔	–
Weight	✔	✔
Country of residence	✔	–
Education, employment, occupation, socioeconomic status	✔	✔ (if changed from baseline)
Family history of PsA and psoriasis	✔	–
Personal history of psoriasis	✔	–
Personal history of PsA and type of PsA	✔	–
Relevant previous and ongoing comorbidities	✔	✔ (if changed from baseline)
Smoking status	✔	✔ (if changed from baseline)
Treatment information		
Previous bDMARD and cs/tsDMARD agents (history)	✔	–
Other treatments for PsA	✔	✔
Treatment exposure details: guselkumab, approved IL-17 inhibitors and other bDMARDs (or cs/tsDMARDs)	✔	✔
Psoriasis therapy: systemic therapies and phototherapy	✔	✔
Laboratory values		
Rheumatoid factor and ACPA[b]	✔	–
CRP	✔	✔
HLA B27 status[b]	✔	–
Latent TB screening and treatment, if available	✔	–
Rheumatologist's assessments		
Changes in PsA/psoriasis and concomitant diseases from baseline	–	✔
Joint counts (66 joint count for swelling and 68 joint count for tenderness)	✔	✔
PGA-PsA	✔	✔
Dactylitis digit count (number of affected digits, 0–20)	✔	✔
LEI score (enthesitis assessment)	✔	✔

Table 2 continued

Assessment	Baseline	Study visit[a]
Presence of nail involvement and number of affected nails (0–20)	✔	✔
BSA	✔	✔
Treatment adherence[c]	✔	✔
ePROs		
EQ-5D-5L	✔	✔
HAQ-DI	✔	✔
PsAID-12	✔	✔
PtGA PsA VAS	✔	✔
Pain VAS	✔	✔
BASDAI	✔	✔
WPAI:PsA	✔	✔
TSQM-9		✔
DLQI	✔	✔
PASS	✔	✔
FiRST	✔	✔[d]
Safety and tolerability assessments		
Adverse events and events of special interest[e]	✔	✔
Concomitant medications for serious adverse events	✔	✔
Study completion/withdrawal		
End-of-study form	–	✔[f]

ACPA anti-citrullinated protein antibody, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *b/cs/tsDMARD* biologic/conventional synthetic/targeted synthetic disease-modifying anti-rheumatic drug, *BSA* body surface area, *CRP* C-reactive protein, *DLQI* Dermatology Life Quality Index, *FiRST* Fibromyalgia Rapid Screening Tool, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *HLA* human leucocyte antigen, *IL* interleukin, *LEI* Leeds enthesitis index, *PASS* patient acceptable symptom state, *PGA-PsA* Rheumatologist's Global Assessment of Disease Activity, *PsA* psoriatic arthritis, *PsAID-12* Psoriatic Arthritis Impact of Disease-12, *PtGA* Patient Global Disease Activity, *TB* tuberculosis, *TSQM* Treatment Satisfaction Questionnaire for Medication, *VAS* visual analogue scale, *WPAI:PsA* Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis

[a]Study visit time points include: month 3 (±3 months), month 6 (±3 months), then every 6 months (±3 months) and at the 'end of treatment' (+1 month) or 'start of treatment' visit (if 2 months have passed since the 'end of treatment' visit)

[b]Any previous result can be used if available in clinical records

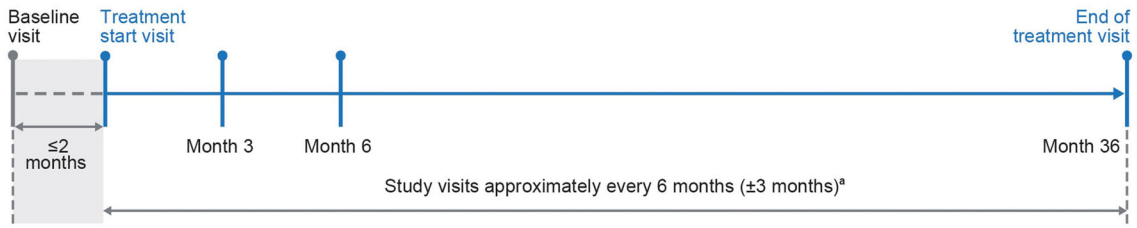
[c]First administration of the drug, last administration before each visit and the approximate number of missed doses since last visit, if this information is available

[d]At first 6-month visit only

[e]Adverse event collection will start from the first administration of an index drug within the study and will stop when a patient completes or leaves the study

[f]At final study visit only

A



Brief overview of data collection in the main study[b]

Assessment	Baseline	Study visit[a]
Patient information	✓	✓ *(if changed from baseline)*
Treatment information	✓	✓
Rheumatologist's assessments	✓	✓
ePROs (EQ-5D-5L, HAQ-DI, PsAID-12, Pain VAS, FIRST, etc.)	✓	✓
Safety and tolerability	✓	✓

B

Brief overview of data collection in the substudy[b]

Measure	Frequency of data collection		
Physical activity, sleep	Continuous (wearable actigraphy device)		
	Daily	Weekly	Monthly
	(smartphone-based app)		
Joint pain map	✓		
Mood, pain, fatigue, skin, morning stiffness scales	✓		
PsA flare	✓		
Sleep and fatigue ePROs		✓	✓
Depression			✓
HAQ-DI[d]			✓
PsAID-12[d]			✓

Fig. 1 Study schedule for **A** participants in the main study and **B** participants in the eDaily by PsABIOnd substudy. [a]After baseline assessment, main study visit time points include: month 3 (±3 months), month 6 (± 3 months), then every 6 months (±3 months) and at the 'end of treatment' (+1 month) or 'start of treatment' visit (if 2 months have passed since the 'end of treatment' visit). [b]See Table 2 (main study) and Table 3 (substudy) for a detailed list of assessments and measures. [c]The baseline period will require a minimum of 9 days of actigraphy data collection (ideally 14 days). [d]Also collected in PsABIOnd main study. *ePRO* electronic patient-reported outcome, *FiRST* Fibromyalgia Rapid Screening Tool, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *PsA* psoriatic arthritis, *PsAID-12* Psoriatic Arthritis Impact of Disease-12, *VAS* Visual Analogue Scale

Table 3 Data collection schedule (eDaily substudy)

	Baseline[a] Weeks −2 to 0	Observation period Weeks 0–24			
		Daily	Weekly	Every 4 weeks	End of substudy[b]
Smartphone app					
Joint pain map	✔	✔	–	–	✔
eDairy with 0–100-point slider scale ratings of mood, pain, fatigue, skin, and morning stiffness duration and severity	✔	✔	–	–	✔
PsA Flare Assessment	✔	✔	–	–	✔
FACIT-F	✔	–	✔	–	✔
PGI-S—Sleep and Fatigue	✔	–	–	✔	–
PGI-C—Sleep and Fatigue[c]	–	–	–	✔	✔
MOS-SS	✔	–	✔	–	✔
HADS	✔	–	–	✔	✔
HAQ-DI[d]	✔	–	–	✔	✔
PsAID-12	✔	–	–	✔	✔
ActiGraph					
Activity (steps, moderate or vigorous physical activity, estimated calories burnt, etc.) and sleep (sleep time, wake time, sleep onset, sleep efficiency, etc.)[e]	continuous				

ePRO electronic patient-reported outcome, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HADS* Hospital Anxiety and Depression Scale, *HAQ-DI* Health Assessment Questionnaire Disability Index, *MOS-SS* Medical Outcomes Study Sleep Scale, *PGI-C* Patient Global Impression of Change, *PGI-S* Patient Global Impression of Severity, *PsA* Psoriatic arthritis, *PsAID-12* Psoriatic Arthritis Impact of Disease-12 Item

[a]The baseline period will require a minimum of 9 days of actigraphy data collection (ideally 14 days)

[b]The end-of-substudy data collection is the last data entry for patients enrolled in the substudy, occurring 24 weeks from the start of treatment (+4 weeks)

[c]PGI-C Sleep and fatigue will be completed at a 4-weekly interval beginning week 4

[d]In Japan, a local version of the HAQ-DI will be used with culturally appropriate modifications of the arising, eating, and reach category questions

[e]Data will be collected continuously in a passive manner via the actigraphy device

Data Collection

Data sources will include validated ePROs and physician-completed assessments (Fig. 1A and Table 2). All physician-completed assessments will be performed using validated assessment tools as per standard of care of patients with PsA by rheumatologists [EULAR and GRAPPA–Outcome Measures in Rheumatology (OMERACT) recommendations]. Site initiation and monitoring activities will aim to ensure standardisation of assessments across participating study sites and countries.

The data collected will be used to calculate composite endpoints, including the clinical Disease Activity Index for Psoriatic Arthritis

(cDAPSA) [19], minimal disease activity (MDA) [20] and very low disease activity (VLDA). If C-reactive protein (CRP) is available, DAPSA and Ankylosing Spondylitis Disease Activity Score–CRP (ASDAS–CRP) will also be calculated. The assessments by the rheumatologist (or trained assessor) will include dactylitis digit count, Leeds Enthesitis Index score, psoriasis body surface area (BSA) and nail involvement (i.e. number of affected nails on hands and feet) (Table 2).

To document treatment persistence, the start and stop date (first and last administration dates) of guselkumab and index IL-17 inhibitor treatments will be recorded for each participant. The stop date will be defined as the date that the last dose of treatment was administered plus one dosing interval (the time between the last treatment and the next scheduled treatment), except when a switch in bDMARD treatment occurs. If a patient switches treatment, treatment persistence will be considered as the time until the next bDMARD treatment is started, if not longer than one treatment dispensing interval between the end of the previous treatment and the start of the new treatment, or until withdrawal or death, whichever occurs first. Treatment adherence for all biological treatments for PsA will be documented through recording treatment continuity at each visit and information on missed doses since last visit.

ePROs will include the Fibromyalgia Rapid Screening Tool (FiRST), EuroQoL 5 Dimension 5-Level (EQ-5D-5L), Health Assessment Questionnaire-Disability Index (HAQ-DI), Psoriatic Arthritis Impact of Disease-12 (PsAID-12), Patient Global Disease Activity Psoriatic Arthritis Visual Analogue Scale (PtGA PsA VAS), Pain Visual Analogue Scale (VAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Work Productivity and Activity Impairment Questionnaire:PsA (WPAI:PsA), 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9), Dermatology Life Quality Index (DLQI) and Patient Acceptable Symptom State (PASS) (Table 2).

Safety data will be collected through reporting adverse events (AEs) and events of special interest at each follow-up visit, from the first use of guselkumab or an IL-17 inhibitor within the study until the participant completes or leaves the study.

Data Analysis

All participants who provide their written consent for data collection and receive guselkumab or an IL-17 inhibitor in this study will be included in the statistical analyses.

Baseline participant and disease characteristics will be summarised using descriptive statistics. Clinical response and effectiveness parameters and observed values as well as changes from baseline will be summarised descriptively at each time point. For continuous/ordinal variables, the number of observations, mean, standard deviation, median, minimum and maximum will be described. For categorical variables, the number, percent, and 95% confidence interval (CI) per category will be summarised. For baseline characteristics and effectiveness endpoints, the summary of continuous/ordinal variables will include the 95% CI of the mean, the summary of categorical variables will include the 95% CI of the proportion.

Because the choice of treatment is at the discretion of the participant's rheumatologist, and not the result of randomisation, any comparison between treatment cohorts will be exploratory in nature. For these comparisons, propensity score (PS) analysis will be used to adjust for relevant observed baseline covariate imbalances. PS stratification (quintiles) and in addition inverse probability of treatment weighting will be used as sensitivity analysis. PS-adjusted comparisons between treatment cohorts will include persistence of initial treatment, achievement of MDA, VLDA, cDAPSA low disease activity (including remission), cDAPSA remission, BSA improvement, and change from baseline in PsAID-12 total and subdomain scores. Persistence time will be compared using PS-adjusted Cox regression analysis. Binomial effectiveness endpoints will be compared using PS-adjusted logistic regression analysis. Continuous effectiveness endpoints will be compared using PS-adjusted multiple linear regression analysis. Results will

be presented as adjusted and unadjusted odds ratios, hazard ratios, or regression coefficients, including 95% CI.

Safety analyses will be descriptive and will include the exposure adjusted incidence and type of AEs, serious AEs, possibly related AEs and related AEs leading to study or treatment discontinuation.

The sample size is not based on an assumed effect size of effectiveness endpoints, rather on providing clinically acceptable 95% CI. The study plans to enrol up to approximately 650 participants receiving guselkumab and approximately 650 participants receiving an IL-17 inhibitor. Therefore, using a conservative response of 50%, a sample size of 650 would give a 95% CI of (46.1%; 53.9%), which would still be considered of clinical interest (sufficiently narrow).

The effectiveness analyses will be performed on the Effectiveness Set, which consists of all enrolled patients without major protocol deviation, with at least one administration of guselkumab or an IL-17 inhibitor during the study who have a visit with any data assessment at baseline and any post-baseline visits. In general, the imputation rules will apply mainly for missing dates.

eDaily by PsABIOnd—an eHealth Substudy

The objective of the eDaily substudy is to explore the associations between actigraphy and ePRO data from the substudy and ePROs from the main study, and between the ePROs and electronic diary (eDiary) for pain, fatigue, mood, skin, morning stiffness and severity used in the substudy and the actigraphy collected measures.

Approximately 150 participants from selected study sites in a number of European countries will be offered entry into the eDaily substudy, which will document the impact of guselkumab or IL-17 inhibitor treatment on patient wellbeing and symptoms using smartphone-based ePRO collection, and continuous activity and sleep measurement using a wearable actigraphy device (Fig. 1B). The enrolment of participants into the substudy will be periodically reviewed to aim for numerically balanced treatment cohorts. The substudy will collect baseline data for 9–14 days before the first administration of the index treatment, followed by a 24-week (+4 weeks) observation period on treatment.

Participants will be included in the substudy if they satisfy all inclusion criteria for the main study, and in addition, if they have agreed to install the smartphone app on their personal smartphone and to complete the substudy assessment and are willing to wear the provided actigraphy device for the duration of their participation in the substudy.

Data for this substudy will be collected using a smartphone-based patient app (eDaily) and a wearable actigraphy device. The medical-grade ActiGraph CentrePoint Insight Watch (CPIW) developed by the ActiGraph corporation will be used according to manufacturer's instructions [21]. The CPIW will continuously capture and record high-resolution tri-axial acceleration data at 32 Hz; data will be transferred from the device to the provider's secure cloud storage in real time over the entire substudy period. Participants will have access to their own data (sleep and physical activity) from the device with a 24–48-h delay for the duration of the study. The eDaily app will capture self-reported joint pain and general pain, mood, fatigue, skin, morning stiffness and presence of PsA flares on a daily basis (eDiary). In addition, participants will be asked to complete ePRO questionnaires in the app on a weekly and monthly basis. A detailed overview of the frequency and timing of data collection in the eDaily substudy is presented in Table 3.

Data collected in eDaily will be analysed using descriptive statistics. For all continuous variables, descriptive statistics will include the number of participants, mean, standard deviation, median, minimum, maximum and 95% CI where applicable. All categorical variables will be summarised using frequencies, percentages and 95% CI, where applicable. Correlations, scatter plots and regressions will be used to investigate the relationship between (1) the ePRO data collected in the main study, (2) the ePRO data collected by means of the

Table 4 Actigraphy endpoints (eDaily substudy)

Endpoint Name	Description
MVPA	Total estimated number of minutes of moderate or higher (moderate to vigorous) physical activity per date as calculated using the Staudenmayer technique
Calories	Total estimated calories burned per date as calculated using the Hildebrand technique
Cutpoints	Breakdown of total min spent per activity category as defined using the Staudenmayer technique
Steps	Total estimated steps take per date
Wear minutes	Total minutes of algorithmically detected "wear time" (Choi technique)
Average awakening	Average length of awakenings in min
Awakening count	The number of awakenings during the sleep period
Efficiency	The ratio between the total sleep time and the total time between the In Bed Time and Out Bed Time
Actual sleep time	The total number of min marked as asleep during the sleep period
Actual wake time	The total number of min marked as awake during the sleep period
Sleep Fragmentation Index	The sum of the percent mobile epochs (movement index) and percent immobile bouts $\leq$ 1 min (fragmentation index) during the sleep period

Standard actigraphy endpoints provided by ActiGraph include those listed above. Additional endpoints may be considered
MVPA moderate to vigorous physical activity

smartphone-based app and (3) various actigraphy measures (daily activity, sleep duration, etc.). Standard actigraphy endpoints are included in Table 4.

Patient Involvement

PsABIOnd was developed in collaboration with a group of representatives of an international patient advocacy group (PAG). During two workshops (advisory boards) held in 2020 and 2021, lead study investigators sought input from PAG representatives on the study design, data collection methods and frequency, acceptability, and patient experience with questionnaires, wearables and mobile devices. PAG representatives reviewed the questionnaires, the time consumption and the wearable actigraphy device. In addition, eDaily by PsABIOnd was developed in collaboration with a group of patients receiving treatment for psoriatic arthritis prescribed by a rheumatologist or dermatologist during advisory boards held in 2021. During the semi-structured interviews, the participants were presented with the solution prototype, lead study investigators sought input from representatives on the app design, data collection methods and frequency, acceptability, and patient experience with questionnaires, wearables and mobile devices. Patients reviewed the questionnaires, the time consumption and the wearable actigraphy device.

Compliance with Ethics Guidelines

This study will be performed in accordance with the Declaration of Helsinki of 1964 and its later amendments. Prior to any data collection or study procedures, the study sponsor, participating rheumatology investigators and study sites will obtain the necessary approvals from their national/local Independent Ethics Committee/Institutional Review Board (IEC/IRB). A list of IECs for those countries in the main study that received ethical approval by 1 September

2022 is included in the Supplementary Material (Supplementary Table 1); a list of IECs for those countries participating in the eDaily substudy is included in the Supplementary Material (Supplementary Table 2). Signed informed consent will be obtained from all patients before enrolment. Participants will be told of the observational nature of the study and that the sponsor only intends to collect information and follow the course of biological treatments of PsA as prescribed in the clinical practice setting. Only patients who are fully able to understand the nature of the study and provide their consent voluntarily will be enrolled. Patients will be informed that their participation in the observational study does not involve any invasive or therapeutic procedures outside of clinical practice, which will continue in accordance with local and overarching guidelines.

Study results will be disseminated at international and regional scientific conferences and via scientific publications in peer review journals. Any scientific presentations or publications will be developed in accordance with Good Publication Practice and International Committee of Medical Journal Editors guidelines. Results will also be posted via the ClinicalTrials.gov website (https://clinicaltrials.gov/ct2/show/NCT05049798).

Current protocol version: Protocol Amendment 2 (CNTO1959PSA4001), 29 April 2022; eDaily by PsABIOnd substudy Protocol Amendment 1 (CNTO1959PSA4001), 8 June 2022.

Strengths and Limitations

One of the key strengths of the PsABIOnd study is its global nature, with the participation of 20 countries across 5 continents. This is unusual for an observational study, which tend to be based on regional data. As a non-interventional study, its limitations include the lack of randomisation, potential effect of bias and missing data. Observational studies have the potential to play a larger role in validating drugs as long as potential biases and confounders are properly addressed. Because the treatments will not be assigned centrally, different treatment cohorts may have imbalances in patient and disease characteristics. Local variability in treatment patterns and local regulatory rules for using index therapies in different global regions may also limit the interpretation of some results. Nevertheless, PsABIOnd will provide important knowledge on the therapeutic effect of guselkumab and IL-17 inhibitors in routine clinical practice. Patients will not be pre-selected and will receive the index therapies regardless of the study, resulting in a more accurate reflection of the real-world patient population than that which can be achieved with RCTs. PsABIOnd will include a large cohort of participants (up to 1300) and will collect data over 36 months, providing valuable information on the long-term safety of these treatments in routine clinical practice. Potentially, specific patterns or subgroups of patients with a preferential response to a given intervention could be detected.

Due to the recent increase in the number of available treatments for patients with PsA, it is becoming more difficult for rheumatologists to make informed treatment decisions for individual patients in their clinical practice. There is a lack of consensus across international guidelines, which can partially be explained by the lack of large prospective head-to-head studies comparing different biological therapies. PsABIOnd will indirectly compare guselkumab with IL-17 inhibitors, treatments that target a regulator and an effector on the IL-23/IL-17 pathway in PsA, during routine clinical practice. Data derived from PsABIOnd will contribute to the knowledge of possible non-overlapping roles these cytokines may have across different disease domains. Similar patient cohorts have previously been enrolled in PsABio [22], a recent real-world study of ustekinumab and TNF inhibitors, applying the same main outcome assessments, meaning that there will be the opportunity to indirectly compare patient outcomes in PsABIOnd with the historical cohorts of PsABio in the future. Given the large amount of information that will be collected both at baseline and during follow-up visits, there is the potential to rank predictors of response to these therapies using new technologies such as machine learning.

Finally, emerging digital health technologies have the potential to collect data outside healthcare settings, capture changes in symptoms on a frequent basis, and thus help generate detailed information on chronic relapsing–remitting diseases such as PsA. eDaily by PsABIOnd—an eHealth substudy, will collect data continuously and/or with high frequency and will generate a between-visits clinical picture of disease and treatment impact on patients with PsA. Examples of additional important clinical information could include the speed of onset of treatment effect, short-term fluctuation in symptoms versus long-term flare-ups. The study is designed as an observational study, so any observations made in eDaily will not be taken into account to modify the routine care of patients taking part in PsABIOnd. However, these results are expected to make an important contribution to the understanding of PsA and may influence patient care in the future.

STUDY STATUS

As of September 2022, 195 participants had been enrolled in the PsABIOnd study: 121 patients in Germany, 30 in the United Kingdom, 16 in Sweden, 14 in Austria, 6 in France, 5 in Spain and 3 in Italy. In the upcoming months, enrolment will start in the remaining participating countries (Argentina, Australia, Belgium, Brazil, Canada, Colombia, Japan, Greece, Mexico, the Netherlands, South Korea, Switzerland and Taiwan). Enrolment for the eDaily by PsABIOnd substudy is expected to start in October 2022.

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Data Availability. Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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