

STATISTICAL ANALYSIS PLAN FOR PROTOCOL P13-990

Observational study in Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) patients to evaluate work productivity before and after the start of adalimumab therapy in daily practice in Belgium (SPACTIVE)

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ABBREVIATIONS

AE	Adverse Event
AS	Ankylosing Spondylitis
ATC	Anatomical Therapeutic Chemical
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BSA	Body Surface Area
CI	Confidence Interval
CRP	C-reactive protein
DAS	Disease Activity Score
DLQI	Dermatology Life Quality Index
EOW	Every Other Week
ESR	Erythrocyte sedimentation rate
HAQ-DI	Health Assessment Questionnaire - Disability Index
HAQ-S	Health Assessment Questionnaire - Spondyloarthritis
ITT	Intention to Treat
MedDRA	Medical Dictionary for Regulatory Affairs
PPS	Per Protocol Set
PsA	Psoriatic Arthritis
PT	Preferred Term
QOL	Quality of Life
SAE	Serious Adverse Event
SOC	System Organ Class
TWPI	Total Work Productivity Impairment
VAS	Visual Analogue Scale
WHO	World Health Organization
WPAI-SHP	Work Productivity and Activity Impairment – Specific Health Problem Questionnaire

1. METHODOLOGY

The purpose of this statistical analysis plan is to provide detailed information on the statistical analysis of the data of study P13-990. The plan is based on the final protocol, incorporating administrative change 1, dated 17 December 2015.

1.1 *Introduction*

Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are both associated with often debilitating clinical symptoms, reduced functional impairment and significant impact on quality of life. As a consequence both diseases imply a significant economic burden, arising from both the direct costs of medical and disability. Health economics data becomes increasingly important to justify the costs of medicines.

Very limited data are available about the employment status and the work productivity of patients with AS and PsA in Belgium. The same is true for the impact of adalimumab treatment on employment status and work productivity.

The aim of this study is to analyse the employment status and work productivity of patients with AS and PsA before and after the start of adalimumab and to look at the relationship between employment status, work productivity, disease activity and clinical evaluations.

1.2 *Study Objectives and Endpoints*

1.2.1 *Study Objectives*

The main objective of the study is to observe in daily practice the evolution of work productivity over 18 months in AS and PsA patients after the start of adalimumab treatment.

The following questions were addressed:

- What is the employment status of AS and PsA patients with active disease before initiation of adalimumab?
- In the patients who work at baseline, what is their work productivity?
- Does adalimumab therapy enable people with AS and PsA to return to work or work more productively?

The secondary objectives are to:

- Investigate if there is a difference in evolution of employment status and work productivity after initiation of adalimumab treatment between AS and PsA patients throughout the study
- Investigate the relationship between disease activity and employment situation and the relationship between clinical evaluations and employment situation at baseline and after 18 months
- Investigate possible correlations between disease activity and work productivity and between clinical evaluations and work productivity

1.2.2 *Study Endpoints*

The primary endpoints is Total Work Productivity Impairment (TWPI) due to AS/PsA:

18 months versus baseline in all patients, measured by the WPAI-SHP questionnaire.
(patient reported outcome)

The secondary endpoints are:

- Total Work Productivity Impairment (TWPI) due to AS and PsA separately: 18 months versus baseline in all patients, measured by WPAI-SHP questionnaire.
(patient reported outcome)
- Evolution over time of (observed for AS and PsA combined and separately) :
 - Number of patients that are employed at each assessed visit
 - Percentage of missed working hours (absenteeism) due to As/PsA 7 days prior to each visit
 - Assessment of the effect of As/PsA on the ability to do regular daily activities during the 7 days prior to each visit (activity impairment)
 - Assessment of the effect of As/PsA on productivity while working during the 7 days prior to each visit (presenteeism)
- Health Related Quality of Life (Patient reported outcome)
 - HAQ-DI (PsA)
 - DLQI (PsA)
 - HAQ-S (AS)
- Disease activity measures and clinical evaluations:
 - DAS28 (PsA)
 - BSA (PsA)
 - BASDAI (AS)
 - Acute phase reactants (CRP / ESR)
 - Physician assessment of disease activity by means of a visual analogue scale (VAS)
 - Patient assessment of disease activity (VAS)
 - Patient assessment of pain (VAS)

1.3 Study Design

The study population consists of adult patients between 18 and 50 years of age, with diagnosed AS / PsA in whom adalimumab treatment was initiated. All medications were prescribed in the usual manner in accordance with the terms of the marketing authorization and in line with the Belgian reimbursement criteria.

The patients provided written informed consent and gave written authorization to the investigator to use and/or disclose personal and/or health data before entry into this observational study.

200 patients were to be enrolled in 20 investigational sites in Belgium during a recruitment period of 12 months. Centers could be University hospitals, regional hospitals, or private practices, with Experience in AS / PsA patient care. Other criteria to be used when selecting investigators were experience and interest to participate in observational studies, sufficient patient potential to include the required number of patients, required availability and resources to participate, and acceptance of the study protocol and study procedures.

Patient data were collected during routine visits at baseline and afterwards preferentially after 3, 6, 12, and 18 months. The total duration of the observation period for the study was therefore approximately 18 months.

This is a local, post marketing, observational study (PMOS). As this is an observational study, no additional visits were required, no study specific medication was provided and no other interventional procedures additional to those comprising routine clinical practice were performed.

All of the following criteria were to be fulfilled to make the patient eligible for the study:

- Inclusion criteria:
 - Age \geq 18 and \leq 50 years
 - Patient diagnosed with AS or PsA
 - Patient newly initiated on adalimumab (according to the Marketing Authorization and Belgian reimbursement criteria)
 - Patient has signed the Informed Consent Form.
- Exclusion criteria:
 - Patients having any of the contraindications mentioned in the SmPC
 - Patients previously treated with biologics
 - Patients participating in other AbbVie-sponsored trials.

A patient was withdrawn from the study if he/she withdrew consent or if the investigator found it no longer appropriate to keep the patient in the study.

1.4 Sample Size Justification

The main objective of this study is to observe the working status in AS and PsA patients before and after the start of adalimumab therapy in daily practice. The primary variable is the change in total work productivity impairment (TWPI) due to AS/PsA between baseline and Month 18. The change will be evaluated in a descriptive way by means of the mean change observed in the study and its 95% confidence interval.

The number of patients to be enrolled (200) was determined on the basis of the recruiting capacity of the participating investigational sites during the foreseen recruitment period of 12 months.

Based on data from Reilly et al¹ it is estimated that about 65% of the patients of the study population are working and therefore evaluable for work productivity impairment.

Supposing that 80% of the employed patients have data available over an 18 month period, the mean change in TWPI will be estimated on the basis of data for about 100 patients.

Based on data for a 16 week treatment period it is estimated that the standard deviation of the change in TWPI will be about 23.8. Since the estimate to be made is for an 18 month treatment period, 95% confidence intervals are also calculated for a somewhat more important standard deviation, arbitrarily set equal to 30.0.

¹ Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993; 4: 353–65.

The table below contains 95% confidence intervals on the mean change for some possible mean changes (-10.0, -15.0 and -20.0), and for standard deviations (SD) of 23.8 and 30.0, supposing data will be available for 100 patients:

Mean change	SD	95% CI
-10.0	23.8	[-14.7 ; -5.3]
-15.0	23.8	[-19.7 ; -10.3]
-20.0	23.8	[-24.7 ; -15.3]
-10.0	30.0	[-16.0 ; -4.0]
-15.0	30.0	[-21.0 ; -9.0]
-20.0	30.0	[-26.0 ; -14.0]

These intervals show that quite precise estimates can be obtained of the change in TWPI on the basis of the planned sample size.

1.5 Study Data Considered for the Analysis

The following data are used for the analysis:

Data only collected at screening (baseline)

- Date of inclusion (screening) and date informed consent form was signed
- Demographic data
 - Year of birth
 - Gender
 - Ethnic origin (Caucasian, Hispanic, Black, Asian, Other).
- Indication for adalimumab therapy (ankylosing spondylitis, psoriatic arthritis) and year of diagnosis.
- Extra-articular disease manifestations: None or
 - Psoriasis
 - Inflammatory bowel disease
 - Uveitis
For each manifestation: Yes/no and (currently active, currently inactive)
- Smoking status (never smoked, ex-smoker, smoker, unknown)
- Other medical history: None or
 - Cardiovascular diseases
 - Cardiovascular risk factors
 - Diabetes
 - Renal disease
 - Hepatic disease
 - Lung disease
 - Mental disorders
 - Other and specification
- Medication history
 - Analgesics
 - NSAIDs

- DMARDs
- Steroids
- Biologic therapy.
- Education background (highest level achieved): None, primary school, secondary school, higher education (non-university), university.
- Start date adalimumab therapy.

Data collected at each visit

- Date of visit
- Employment situation (to be answered at baseline, and at each follow-up visit in case of any change since the last visit):
 - Current employment status:
 - Housewife/houseman, due to As/PsA (yes, no)
 - Unemployed, due to As/PsA (yes, no)
 - Retired, due to As/PsA (yes, no)
 - Part-time employed: Percentage, due to As/PsA (yes, no)
 - Full-time employed
 - Student.
 - Current job content:
 - Professional or technical
 - Administrative or managerial
 - Sales
 - Service tasks
 - Agricultural
 - Production/manufacturing, transport equipment operator, laborer
 - Armed forces
 - Other and specification.
 - Current occupational situation:
 - Employee
 - Independent
 - Public/civil servant
 - Volunteer
 - Other
- Disease activity measures and clinical evaluations:
 - Only PsA
 - Body Surface Area (BSA) affected (no psoriatic lesions, <3%, 3-10%, 11-20%, >20%).
 - DAS28 score.
 - Only AS
 - BASDAI
 - Consists of 6 items assessed on ordinal scales. Higher scores indicate higher severity. The scores for Items 1 to 5 are integers between 0 and 10. The scores for Item 6 is a continuous assessment between 0 and 10.
 - The total score is calculated as:
[(Item 1+Item 2+Item 3+Item 4)+(Item 5+Item 6)/2]/5

PsA and AS

- Physician's global assessment of disease activity by means of a 100 mm VAS (0=no disease activity, 100=maximal disease activity).
- Patient's global assessment of disease activity by means of a 100 mm VAS (0=no disease activity, 100=maximal disease activity).
- Patient's global assessment of pain by means of a 100 mm VAS (0=no pain, 100=serious pain).
- Acute phase reactants:
 - o Recent ESR (mm/h)
 - o Recent CRP (mg/dl).
- Health-related Quality of Life (QOL):
 - Only PsA*
 - DLQI consisting of 10 questions.
 - o For all 10 questions except question 7 the answers are coded as 0=not at all, 1=a little, 2=a lot, 3=very much. The answer 'not relevant' (questions 3, 4, 5, 6, 8, 9, and 10), and an unanswered question are coded as 0.
 - o Question 7 consists of 2 parts:
 - An answer 'yes' to the first part is coded as 3 (very much).
 - In case of an answer 'no' or 'not relevant' to the first part or if the first part is unanswered the following codes are used for the answer to the second part: 0=not at all, 1=a little, 2=a lot.
 - In case the first part is answered 'no' or 'not relevant' or is unanswered, and the second part is unanswered the score is 0.
 - HAQ-DI consisting of 20 questions coded as 0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do. The questions are divided into the following categories:
 - o Dressing and grooming: Questions 1, 2
 - o Arising: Questions 3, 4
 - o Eating: Questions 5, 6, 7
 - o Walking: Questions 8, 9
 - o Hygiene: Questions 10, 11, 12
 - o Reach: Questions 13, 14
 - o Grip: Questions 15, 16, 17
 - o Common daily activities: 18, 19, 20.

Only AS

- HAQ-S consists of 3 parts:
 - o 25 questions coded as 0=without any difficulty, 1=with some difficulty, 2=with much difficulty, 3=unable to do. The first 20 questions are almost identical with the 20 questions of the HAQ-DI questionnaire and divided into the same categories. Questions 21, 22, and 23 are regrouped into a separate (9th) category ('other daily activities'), and questions 24 and 25 belong to the additional (10th) category 'driving a car'. Furthermore, use of devices can be indicated (7 for categories 1 to 4, and 6 for categories 5 to 9), and the need of outside help can be indicated for 4 items (hygiene, reach, grip and opening, and errands and chores).
 - o 1 question assessed on a 5 point ordinal scale (entirely, usually, moderately, a bit, not at all), concerning the possibility of performing daily activities such as going for a walk, going up stairs, carrying errands, and moving a

chair.

- 3 additional items evaluating pain during the past week on a scale from 0 (no pain) to 100 (severe pain), general health on a scale from 0 (very good) to 100 (very bad), and stiffness on a VAS (with 0 mm=not stiff, 100 mm = very severe stiffness).

PsA and AS

- Work Productivity and Activity Impairment – Specific Health Problem (WPAI-SHP) questionnaire at baseline and each follow-up visit:
 - Q1: Do you presently have a professional activity? (yes, no).
 - In case the subject has a professional activity:
 - Q2: Number of hours work missed during the past 7 days due to the disease.
 - Q3: Number of hours work missed during the past 7 days due to other reasons.
 - Q4: Number of hours worked during the past 7 days.
 - Q5: In case the subject worked during the past 7 days (number of hours worked >0): To what extent did the disease decrease productivity?: 0=no effect, to 10=could not work at all.
 - Q6: To what extent did the disease decrease the capacity to perform usual daily activities?: 0=no effect, to 10=could not perform any daily activities.
- Adalimumab treatment recorded at each follow-up visit:
 - Was there any change in adalimumab treatment? (yes, no)
 - In case of change this was to be recorded in the adalimumab treatment section with for each treatment period: Type (pen or syringe), dose, frequency (EOW or other), start and stop date (or ongoing at end of study).
- Other AS/PsA treatment:
 - Drug name.
 - Dose and frequency.
 - Start date, and stop date or ongoing.
- Serious adverse events (SAEs):
 - Event description.
 - Final diagnosis.
 - Onset date.
 - End date if recovered.
 - Serious (yes, no), and if yes, criterion for seriousness (hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, life threatening, death and date, congenital anomaly, medically important event, elective abortion, miscarriage).
 - Causality with adalimumab (probable, possible, probably not related, not related, not assessable).
 - Action taken after the event (adalimumab dosage increased, adalimumab dosage decreased, none, adalimumab discontinuation).
 - Outcome (recovered, not recovered, recovering, improved, worsened, death, unknown, recovered with sequelae and specification).

Study termination

- Study completion or study withdrawal date.
- Reason for study termination:
 - Study completion
 - Withdrawal of consent.
 - Lost to follow-up.
 - Discontinued due to administrative reasons.
 - Death.
 - Serious adverse event.
 - Discontinued due to other reason.

1.6 Derived Variables

- Age (years) = year of inclusion – year of birth
- Study duration (month) =
$$12 \times (\text{date patient completed study/withdrew} - \text{date of inclusion}) / 365.25$$
- Adalimumab treatment duration (month) =
$$12 \times [\text{first of (last stop date adalimumab and date patient completed study/withdrew)} - \text{start date adalimumab} + 14] / 365.25$$
- BASDAI total score = [(Item 1+Item 2+Item 3+Item 4)+(Item 5+Item 6)/2]/5:
If one of items 5 or 6 is missing the other is considered.
If one of items 1, 2, 3, 4, or the average of 5 and 6 is missing, the missing item is estimated by the average of the available among items 1, 2, 3, 4, and the average of items 5 and 6. If more than one of these is missing, the total score is missing.
- BASDAI category (axial disease):
 - Yes: BASDAI total score >4
 - No: BASDAI total score ≤ 4 .
- HAQ-DI
Each of the 8 categories is given a score by taking the maximum score of all questions in the category (question in each category with the highest score is the score for that category).
The HAQ-DI will be calculated by dividing the sum of the category scores by the number of categories with at least 1 question answered. If fewer than 6 categories have responses, no disability score will be calculated. The HAQ-DI score ranges from 0 to 3. A lower HAQ-DI disability score indicates better function.
- HAQ-S
Each of the 10 category is given a score by taking the maximum score of all questions in the category (question in each category with the highest score is the score for that category). If the maximum score equals 0 or 1, but a device related to that category is used, or help from another person is provided for the category, then the category score is increased to 2. If the category score is already 2, and a device related to that category is used, or help from another person is provided for the category, the score for that category remains 2. The table below details how each aid and device is associated with the category scores.

If all questions within a given category are unanswered, no score will be provided for that category. The HAQ-S will be calculated by dividing the sum of the category scores by the number of categories with at least 1 question answered. If fewer than 6 categories have responses, no disability score will be calculated. The HAQ-S score ranges from 0 to 3. A lower HAQ-S disability score indicates better function.

NOTES:

- The assignment of aids and devices to categories is done as follows:

Aid or device	Associated with category
Cane, walker, crutches, wheelchair	Walking
Devices used for dressing	Dressing and grooming
Built up or special utensils	Eating
Special or built up chair	Arising
Raised toilet seat	Hygiene
Bath tub seat	Hygiene
Jar opener (for jars previously opened)	Grip
Bath tub bar	Hygiene
Long-handled appliances for reach	Reach
Long-handled appliances for bathroom	Hygiene

- No aids or devices are assigned to the category 'Activities'.
- Aids and devices specified in the 'Other' field will not be used in the calculations.
- Help from another person for errands and chores is assigned to the category 'Activities'.
- Help from another person for gripping and opening things is assigned to the category 'Grip'.
- WPAI Questionnaire:
 - Absenteeism = Percentage work time missed due to disease = $100 \times Q2 / (Q2+Q4)$
 - Presenteeism = Percentage impairment while working due to the disease = $100 \times Q5 / 10$
 - Total work productivity impairment (TWPI) due to disease = Absenteeism (%) + extent to which the disease decreased productivity (%) x [number of hours worked /(number of hours work missed due to the disease + number of hours worked)] = $100 \times Q2 / (Q2+Q4) + 100 \times [1 - Q2 / (Q2 + Q4)] \times [Q5 / 10]$
 - Percentage activity impairment due to disease = Extent to which the disease affected the ability to perform usual daily activities = $100 \times Q6 / 10$
- Dermatology Life Quality Index (DLQI) questionnaire
 - In case one question is unanswered it is given a score of 0. In case 2 or more questions are unanswered the DLQI score is not calculated. Question 7 is considered unanswered if both parts are unanswered.
 - The DLQI score is calculated as the sum of the scores of the individual questions.

- DLQI category
 - o 0-1: No effect
 - o 2-5: Small effect
 - o 6-10: Moderate effect
 - o 11-20: Very large effect
 - o 21-30: Extremely large effect.
- Regrouped DLQI category
 - o ≤ 5
 - o > 5
- DLQI scales
 - o Symptoms and feelings: Sum of scores of Questions 1 and 2
 - o Daily activities: Sum of scores of Questions 3 and 4
 - o Leisure: Sum of scores of Questions 5 and 6
 - o Work and school: Score of Question 7
 - o Personal relationships: Sum of scores of Questions 8 and 9
 - o Treatment: Score of Question 10.

NOTES:

1. If any question associated with a scale is unanswered the corresponding scale is not calculated.
 2. If 2 or more response options are ticked, the highest score is recorded.
 3. In case of a response between 2 tick boxes, the lower score is recorded.
- Serious Adverse Events (SAEs)
 - SAEs are coded by AbbVie using the Medical Dictionary for Regulatory Activities (MedDRA). One or more Preferred Terms (PT) are associated with each SAE. These terms will be provided to DICE who will map them to the corresponding System Organ Class (SOC).
 - Study-emergent SAE: An SAE is considered study-emergent if its onset date is on or after the date of informed consent and at most 70 days after the date of last administration of adalimumab.
 - Relation of SAE with study medication:
 - o Related: Probably related, possibly related, probably not related, unknown, not reported, missing.
 - o Not related: Not related.
 - Non-Serious Adverse Events (AE)
The CRF allowed the reporting of non-serious adverse events. These events are coded using MedDRA Version 20.0.
 - AS/PsA treatments recorded at baseline and during the study are coded using the World Health Organization (WHO) Drug Dictionary, Version 1 December 2011.

1.7 Statistical Methodology

The analysis will consist of data descriptions and statistical hypothesis testing. Throughout this document, the following terminology is used for indicating the type of descriptive analysis to be performed:

- ‘Descriptive statistics’ is used to indicate the description to be provided for quantitative variables, and includes the mean, standard deviation, 95% confidence interval (CI) on the mean, minimum, 1st quartile, median, 3rd quartile, maximum,

- number of available observations, and number of missing observations.
- ‘Frequency distribution’ is used to indicate the description to be provided for categorical variables and consists of numbers and percentages for each of the scores or categories.

For the variables recorded for both AS and PsA patients the descriptions will be given for all patients as well as separately for each subgroup.

The relationship between TWPI and disease activity at baseline and between TWPI and clinical evaluations at baseline will be evaluated by means of the Spearman rank correlation coefficient.

The relationship between work status and disease activity and between work status and clinical evaluations will be evaluated by means of analysis of variance, controlled for indication, if applicable.

1.8 Patient Population

The following analysis sets are considered for the analysis:

Intention to Treat (ITT) Set: All patients enrolled in the study, who received at least one dose of adalimumab, and for whom any follow-up data are available.

Per Protocol Set (PPS): All patients of the ITT Set without any major protocol deviations. Protocol deviations will be reviewed and classified as minor or major during a data review that will be held before database lock.

Safety Set: All patients enrolled in the study, who received at least one dose of adalimumab, and for whom any follow-up data are available.

All baseline and efficacy data will be analysed on the basis of the PPS. In case the difference between the ITT Set and PPS exceeds 10% of the patients of the PPS, the TWPI data will also be analysed for the ITT Set.

The analysis of adverse events and of the course of the study will be performed on the basis of the Safety Set.

1.9 Data Handling

The following data handling transformations are performed for the analysis:

Onset data

- Date of enrolment is taken to be date of informed consent

WPAI Questionnaire

- For patients with (number of hours missed due to psoriasis = number of hours worked = 0), Absenteeism, Presenteeism and Total work productivity impairment are set to missing.
- If the answer to Question 1 of the WPAI Questionnaire is not YES but there is an answer to any of Questions 2, 3, 4, or 5, then the answers to these questions are considered to be missing.

Serious Adverse Events

In case of a partial or missing date for the start of a serious adverse event it will be

assumed that the event was study-emergent unless it can be determined from the partial start or stop date that the event definitely started before the date of informed consent or more than 70 days after the last administration of study medication.

Last Observation and Last Attended Visit

The analysis of individual scales is performed for each visit and for the last observation after baseline. For multi-item questionnaires the last observation after baseline is defined as the observation for the last visit after baseline at which any of the items of the questionnaire is completed.

The analysis of the relation between variables is performed for data recorded at baseline, at Month 18, and at the last attended visit.

Other Missing Data

No other estimation will be performed of missing data. In order to obtain estimates for the end of the study, use is made of the last observation after baseline. If date of completion/withdrawal was missing it has been set to date of last contact.

1.10 Changes from the Analysis Foreseen in the Protocol

For the DLQI the protocol only foresaw an analysis of the total score and the categories. In order to provide additional information descriptions will also be provided for the 6 scales of the DLQI, and for the regrouped categories ≤ 5 and > 5 .

The protocol foresaw to analyse the evolution of the work productivity data, the health-related quality of life scores, and the disease activity measures and clinical evaluations based upon the data collected in time windows around the foreseen study visits. Since data were collected in the CRF around the planned visits, it was decided to analyse the data by reported study visit.

Since an important proportion of patients dropped out before the Month 18 visit it was decided also to perform analyses for the last observation after baseline.

The protocol did not foresee to perform an analysis of the safety data. It was decided to perform an analysis of adverse events and of the course of the study and for this purpose a safety analysis set was defined.

In order to better comprehend the effect of employment status it was decided to provide frequencies of extra-articular disease manifestations broken down by employment status.

The protocol foresaw to primarily perform the analysis on the basis of the PPS and to perform a sensitivity analysis of the TWPI on the ITT Set. It was decided only to perform the latter analysis in case the difference between the two analysis sets exceeds 10% of the patients of the PPS.

2. SAMPLE DESCRIPTION

2.1 Study Population

- Number of patients in the ITT Set and the PPS, and number of patients in the ITT Set and the PPS broken down by indication.

2.2 Study Period

For all patients enrolled:

- Date of first and last inclusion, data of last study completion/withdrawal.

3. ONSET DATA

The analysis is performed for all patients and broken down by indication.

3.1 Demographic Data

- Descriptive statistics for age.
- Frequency distribution for gender and ethnic origin.

3.2 Medical Data

- Frequency distribution for indication for adalimumab therapy.
- Frequency distribution for each extra-articular disease manifestation (psoriasis, inflammatory bowel disease, uveitis).
- Frequency distribution for combinations of extra-articular disease manifestations.
- Frequency distribution for combinations of extra-articular disease manifestations broken down by employment status.
- Frequency distribution for combinations of currently active extra-articular disease manifestations.
- Frequency distribution for combinations of currently active extra-articular disease manifestations broken down by employment status.
- Frequency distribution for smoking status.
- Frequency distribution for each type of other medical history (cardiovascular diseases, cardiovascular risk factors, diabetes, renal disease, hepatic disease, lung disease, mental disorders, other).
- List of items of other medical history.
- Frequency distribution for each type of medication (analgesic, NSAID, DMARD, steroid, biologic therapy).
- Frequency distribution for combinations of types of medication.

3.3 Educational Background and Employment Situation

- Frequency distribution for highest educational level achieved.
- Frequency distribution for current employment status.
- For housewife/houseman, unemployed, retired, part-time employed, frequency distribution for whether it is due to the disease.
- Frequency distribution for current job content.
- Frequency distribution for current occupational situation.

4. COURSE OF THE STUDY

The analysis is performed for all patients and broken down by indication.

Study duration and study termination

- Descriptive statistics for study duration.
- Frequency distribution for reason for study termination.

Adalimumab treatment

- Descriptive statistics for treatment duration.
- Frequency distribution of any change in adalimumab treatment.
- For the patients for whom any change in adalimumab treatment was recorded, list of the data recorded concerning adalimumab treatment.

Concomitant Medications

- Frequency distribution of subjects taking other AS/PsA medication by WHO-DRUG anatomical class.
- Frequency distribution of subjects taking other AS/PsA medication by WHO-DRUG anatomical and therapeutic class.

Employment Situation

- Frequency distribution of any change in employment situation.
- For the patients for whom any change in employment situation was recorded, list of the data recorded at each visit concerning employment situation.

5. EFFICACY DATA

5.1 WPAI Questionnaire

- Frequency distribution of professional activity at baseline, at each visit, and at the last observation.
- Frequency distribution of professional activity at each visit and at the last observation, broken down by professional activity at baseline.

For absenteeism, presenteeism, TWPI, and percentage activity impairment:

- Descriptive statistics at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change between baseline and each visit, and between baseline and the last observation.

5.2 DAS28 (PsA)

- Descriptive statistics of the DAS28 score at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in DAS28 score between baseline and each visit, and between baseline and the last observation.

5.3 BSA (PsA)

- Descriptive statistics of BSA at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in BSA between baseline and each visit, and between baseline and the last observation.

5.4 DLQI Questionnaire (PsA)

- Descriptive statistics of the DLQI score at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in DLQI score between baseline and each visit, and between baseline and the last observation.
- Descriptive statistics of each DLQI scale at baseline, at each visit and at the last observation.
- Descriptive statistics of the change in each DLQI scale between baseline and each visit, and between baseline and the last observation.
- Frequency distribution of the DLQI category at baseline, at each visit, and at the last observation.
- Frequency distribution of the regrouped DLQI category at baseline, at each visit, and at the last observation.
- Frequency distribution of the regrouped DLQI category at each visit, and at the last observation, broken down by the regrouped DLQI category at baseline.

5.5 HAQ-DI (PsA)

- Descriptive statistics of the HAQ-DI score at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in the HAQ-DI score between baseline and each visit, and between baseline and the last observation.

5.6 BASDAI (AS)

- Descriptive statistics of the BASDAI total score at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in BASDAI total score between baseline and each visit, and between baseline and the last observation.
- Frequency distribution of the BASDAI total score category (axial disease) at baseline, at each visit, and at the last observation.
- Frequency distribution of the BASDAI total score category (axial disease) at each visit and at the last observation, broken down by the BASDAI total score (axial disease) at baseline.

5.7 HAQ-S (AS)

- Descriptive statistics of the HAQ-S score at baseline, at each visit, and at the last observation.
- Descriptive statistics of the change in the HAQ-S score between baseline and each visit, and between baseline and the last observation.
- Frequency distribution of the possibility of performing daily activities at baseline, at each visit, and at the last observation.
- Frequency distribution of the possibility of performing daily activities at each visit and at the last observation, broken down by the possibility of performing daily activities at baseline.
- Descriptive statistics of the HAQ-S additional items (pain, general health, stiffness) score at baseline, at each visit and at the last observation.
- Descriptive statistics of the change in the HAQ-S additional items between baseline and each visit, and between baseline and the last observation.

5.8 Physician and Patient Assessments of Disease Activity and Patient Assessment of Pain

- Descriptive statistics at baseline, at each visit and at the last observation.
- Descriptive statistics of the change between baseline and visit, and between baseline and the last observation.

5.9 Acute Phase Reactants

- Descriptive statistics at baseline, at each visit and at the last observation.
- Descriptive statistics of the change between baseline and each visit, and between baseline and the last observation.

5.10 Relation Between Work Status and Clinical Evaluations

For DAS28 score, BSA, DLQI score, HAQ-DI score, BASDAI total score, HAQ-S (total score and scores for pain during the past week, general health, and stiffness), physician and patient assessments of disease activity, and patient assessment of pain:

- For baseline, Month 18, and the last attended visit:
 - Descriptive statistics broken down by work status (Q1 of the WPAI).
 - Evaluation of the effect of work status (and indication) by means of analysis of variance.
- For the change between baseline and Month 18, and between baseline and the last attended visit, descriptive statistics broken down by work status (Q1 of the WPAI) at baseline.

5.11 Relation Between Work Productivity and Clinical Evaluations

For baseline, the change between baseline and Month 18, and the change between baseline and the last attended visit, Spearman rank correlation between:

- Absenteeism, presenteeism, TWPI, percentage activity impairment and
- DAS28 score, BSA, DLQI score, HAQ-DI score, BASDAI total score, HAQ-S scores (total score and scores for pain during the past week, general health, and stiffness), physician and patient assessments of disease activity, patient assessment of pain.

6. SAFETY DATA

6.1 Serious Adverse Events

- By-patient list of individual data for SAEs that are not study-emergent.
- By-patient list of individual data for study-emergent SAEs.
- Frequency distributions of patients with study-emergent SAEs¹, and with study-emergent SAEs causing treatment discontinuation.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC and PT¹.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC, PT, and maximal severity.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC, PT, and strongest relationship.

6.2 Non-Serious Adverse Events

- By-patient list of individual data for non-serious AEs that are not study-emergent.
- By-patient list of individual data for non-serious study-emergent AEs.
- Frequency distributions of patients with non-serious study-emergent AEs, and with non-serious study-emergent AEs causing treatment discontinuation.
- Frequency distributions of patients with non-serious study-emergent AEs in PTs for which the frequency of non-serious study-emergent AEs exceeds 1%¹.
This table will be titled ‘Patients with study-emergent non-serious adverse events above the frequency threshold (1%)’.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC.
- Frequency distributions of patients with study-emergent SAEs by MedDRA SOC and PT¹.

¹ Information will also be reported in dedicated data files in order to report to ClinicalTrials.gov.