1.0 Title Page

AbbVie SA

Post Marketing Observational Study 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)

Product Name:	Adalimumab
Type of Study:	Post-marketing Observational Study (PMOS)
Date:	06 December 2012
Biometrics:	██████████████████████████████
Sponsor:	AbbVie SA ███████████
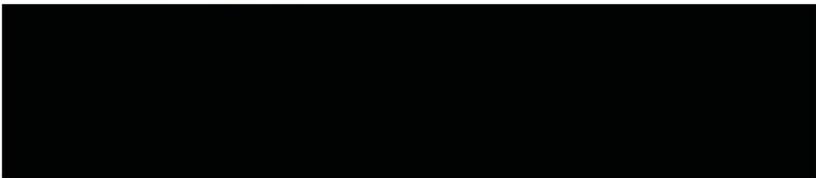
This study will be conducted in compliance with this protocol.

Confidential Information

No use or disclosure outside AbbVie is permitted without prior written authorization from AbbVie.

2.0   Table of Contents

3.0   Introduction

Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are the major subtypes of rheumatic diseases named as spondyloarthritides (SpAs). The most important clinical features of this group are inflammatory back pain, asymmetric peripheral oligoarthritis, predominantly of the lower limbs, enthesitis and specific organ involvement such as anterior uveitis and chronic inflammatory bowel disease.

3.1.   Ankylosing spondylitis

Ankylosing spondylitis (AS) is the prototype of SpAs and primarily affects the axial skeleton, with a characteristic involvement of the spine and sacroiliac joints, synovitis of peripheral joints may occur as well. Pain, stiffness due to inflammation and progressive spinal ankylosis that may lead to complete spine rigidity (total spinal ankylosis) are the clinical hallmarks of the disease. Inflammation may also affect entheses, heart, lung, intestine and eyes. The prevalence of AS appears to be substantially higher than previously estimated, approximating 0.9% in Caucasians (1). This resembles the prevalence of rheumatoid arthritis (RA), but unlike RA, AS is more common in men than in women. The average age at onset of AS is in the third decade, which can necessitate treatment for several decades. In addition, due to the early onset, development of functional disability and life-time costs, the socioeconomic impairment for subjects with active AS is likely to be high. Recent surveys have shown that AS is associated with a comparable disability to that observed in RA with substantial direct and indirect costs (2).

Work disability in AS and its costs

Due to its early onset, chronicity and consequent functional impairment, AS carries a significant economic burden, arising from both the direct costs of medical and disability care and from indirect costs associated with loss of earnings and decreased productivity. The prevalence of work disability in AS patients was found to range from 13 - 46% (3-7).

A Dutch study reported a significant 11%-reduction in overall participation in the labor force, compared with the age matched general population. More than 75% of patients with AS who had stopped working were officially recognized as work disabled (8). The withdrawal rates from work in patients with AS were reported to be about 3-times higher than in the general population (9). Data from a Swedish Registry showed that AS patients have an increased risk of sick leave, with a relative risk of 1.8 and median of 30 additional sick days per year compared with population-based controls (10). A UK-based study suggested that 50% of AS patients at working age lost their job due to AS activity, and of those in work 50% were work unstable, at moderate or high risk of job retention problems (11). The society costs of lost productivity due to AS were estimated at 3.595 EUR per patient per year (12).

Treatment of AS

Nonsteroidal anti-inflammatory drugs (NSAIDs) and physical modalities are the current standard therapy for AS. Evidence exists that NSAIDs treat the symptoms of AS, but it has not been confirmed that NSAID therapy reliably influences spinal mobility, acute phase reactants (e.g., ESR and CRP) or the long-term disease course with respect to the development of ankylosis (13, 14).

The advent of tumour necrosis factor α (TNF-α) blockade marks the first major therapeutic advance in AS since the introduction of NSAIDs. Treatment with anti-TNF-α agents has been proven to provide significant improvements in clinical symptoms, physical function and patients' health related quality of life (15).

Of the available TNF-α antagonists, adalimumab is the first fully human monoclonal antibody that binds with a high affinity to both free serum and membrane bound TNF-α. Adalimumab therapy has been proven to effectively and long-term reduce the signs and symptoms of AS (16, 17), including in patients with total spinal ankylosis (18), and extra-articular manifestations, such as uveitis (19). Treatment with adalimumab also significantly improved physical health status and quality of life (20). A recent post-hoc

analysis of ATLAS trial (16), which was basically aimed at assessing the factors associated with work ability and disability in patients with AS, also demonstrated that adalimumab sustains improvements in work outcomes, as measured by Work Productivity and Activity Impairment – Specific Health Problem Questionnaire (WPAI-SHP) (21). Due to the study design, however, these findings did not allow for a definite conclusion that the improvements in work outcomes were a direct result of adalimumab therapy (21).

3.2.   Psoriatic arthritis

Psoriatic Arthritis (PsA) is an inflammatory arthropathy that occurs in up to one third of patients with psoriasis and is usually diagnosed years after the appearance of psoriatic skin disease, but may also precede it.

Synovitis of peripheral joints is a major feature of PsA, and joint affection can be monoarthritic, oligoarthritic, or polyarthritic. More than half of patients with PsA exhibit progressive, erosive arthritis that often is associated with functional impairment. PsA may also affect the axial skeleton: the spine can be involved in any part, most often at the lumbosacral transition and the neck.

PsA can develop at any time, but for most people it appears between the ages of 30 and 50, and it affects men and women equally. The overall prevalence of PsA is approximately 0.1% (22, 23).

Work disability in PsA and its costs

There is a dearth of published pharmacoeconomic studies in PsA, despite increasing evidence that affected patients can have significant radiographic joint damage, functional impairment, reduced quality of life (QoL) and long-term work disability. Among patients treated with anti-TNF agents and registered in the British Society for Rheumatology Biologic Register, work disability rates were 39% for PsA patients, 41% for AS patients and 49% for those with RA (24). Somewhat lower rates were reported for Norwegian PsA

patients on either conventional or biologic DMARD (disease modifying anti-rheumatic drugs) therapy: work disabled were 32.7% of females and 17.4% of males (25).

Treatment of PsA

The treatment of PsA is directed at controlling the inflammatory process. Although there is no clear correlation between the skin and joint inflammation in every patient, the skin and joint aspects of the disease need to be treated simultaneously. Initial treatment consists of NSAIDs for joint disease and topical or systemic therapy for the skin. More severe disease is likely to require treatment with DMARDs, such as MTX, and intra articular steroids. Among second-line treatments used in RA and evaluated in patients with PsA are sulfasalazine, MTX, leflunomide, gold, antimalarials, cyclosporine, and azathioprine (26).

Anti-TNF agents are highly effective in treating the signs and symptoms of PsA, including dactylitis and enthesitis, and they also suppress structural joint damage and treat skin psoriasis (27).

Treatment with adalimumab, dosed at 40 mg s.c. every other week, showed in placebo controlled clinical trials ACR20 response rates of 39-58% and ACR50 response rates of 25-39% in patients with active PsA who had failed previous standard therapy (45, 46). Significant improvements of psoriatic skin changes and disease-related quality of life were also noted (28).

Data on the impact of biologic therapy on work disability and productivity in patients with PsA are scarce. A study that determined the cost-effectiveness of anti-TNF treatment in patients with RA, PsA and AS in a real-world setting found that the number needed to treat (NNT) in order to achieve the minimal clinically important difference in HAQ score (decrease by ≥ 0.2) was about 2 for all three evaluated diseases: 1.94 for RA, 1.88 for PsA and 2.30 for AS (29). After 14 weeks of treatment with infliximab, median productivity as measured on a 0 to 10 visual analog scale improved significantly compared with the placebo group (30). Results of the recently published ACCLAIM study in patients with

PsA on adalimumab therapy demonstrated significant improvements (decreases) from baseline to week 12 in 3 of the 4 domains assessed by the Work Limitations Questionnaire (WLQ): Physical, Time and Output (31).

4.0 Rationale

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.

5.0 Study Objectives

5.1 Primary Objective

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 will be 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?

5.2   Secondary Objectives

- 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

5.3   Primary endpoints:

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)

5.4   Secondary endpoints:

- 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

- - o Percentage of missed working hours (absenteeism) due to As/PsA 7 days prior to each visit
  - o 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)
  - o 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)
  - o HAQ-DI (PsA)
  - o DLQI (PsA)
  - o HAQ-S (AS)
- Disease activity measures and clinical evaluations:
  - o DAS28 (PsA)
  - o BSA (PsA)
  - o BASDAI (AS)
  - o Acute phase reactants (CRP / ESR)
  - o Physician assessment of disease activity (VAS)
  - o Patient assessment of disease activity (VAS)
  - o Patient assessment of pain (VAS)

6.0 Investigational Plan

6.1 Selection of Study Population

The study population will consist of adult patients with diagnosed AS / PSA in whom adalinumab treatment will be initiated. All medications will be prescribed in the usual manner in accordance with the terms of the marketing authorization and in line with the Belgian reimbursement criteria.

The patients must provide written informed consent prior to study participation and must give written authorization to the investigator to use and/or disclose personal and/or health data before entry into this observational study.

6.1.1 Inclusion Criteria

- Patients ≥18 years and ≤ 50 years
- Diagnosed with AS or PsA
- Patient newly initiated on adalimumab (according to the Marketing Authorization and Belgian reimbursement criteria)
- Signed Informed Consent

6.1.2 Exclusion Criteria

- Any contraindication for adalimumab as specified in the corresponding SmPC
- Patients previously treated with biologics
- Patients participating in other AbbVie-sponsored trials

6.2 Number of Patients to be Enrolled

It is anticipated to enroll 200 patients in the study. Patients will be enrolled by approximately 25 centers in Belgium. Each centre will include on average 8 patients during the 12 month recruitment period.

6.3 Investigator Selection Criteria

Approximately 20 centers across Belgium will be asked to participate in this study. Centers can be University hospitals, regional hospitals, private practices.

Following criteria will be used when selecting investigators:

- Experience and interest to participate in observational studies
- Experience in AS / PsA patient care

- Sufficient patient potential to include the required number of patients in the study
- Required availability and resources to participate in this observation study
- Acceptance of study protocol and study procedures

6.4   Study Duration

Data will be collected during routine visits at baseline and afterwards preferably after 3, 6, 12 and 18 months. The total duration of the observation period for the study will therefore be approximately 18 months.

Patients can be withdrawn from the study at any time during the study when the patient withdraws his/her consent or if the investigator finds it no longer appropriate to keep patients in the study.

6.5   Study Conduct

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

6.5.1   Product Supply

Not applicable.

6.5.2   Description of Activities

The following procedures will be performed
Screening :

- Patient information will be explained to the patient and Informed Consent will be signed

- Inclusion/Exclusion criteria will be checked

Baseline :

Following information (if available) will be collected during the visit:
- Medical history
- Demographics (gender, year of birth, race)
- AS and/or PsA diagnosis
- Previous & current AS and PsA treatments up to 1 month before inclusion
- Extra-articular disease manifestations (psoriasis, inflammatory bowel disease, uveïtis)
- Educational background
- Employment situation
- Disease activity measures and clinical evaluations :

  For PsA patients
  - DAS28
  - BSA
  - Physician assessment of disease activity (VAS)
  - Patient assessment of disease activity (VAS)
  - Patient assessment of pain (VAS)
  - Acute phase reactants (CRP / ESR)

  For AS patients
  - BASDAI
  - Physician assesment of disease activity (VAS)
  - Patient assesment of disease activity (VAS)
  - Patient assessment of pain (VAS)
  - Acute phase reactants (CRP / ESR)
- Health related Quality of Life (patient reported outcome) :

  For PsA patients
  - DLQI
  - HAQ - DI

For AS patients
- HAQ-S
- WPAI-SHP (PRO)
- Serious adverse events

Routine visits (by preference at month 3, 6, 12, 18):

- Following information (if available) will be collected during the visit:
- Changes in AS and PsA treatment since previous visit
- Change in employment situation
- Disease activity measures and clinical evaluations :

For PsA patients
- DAS28
- BSA
- Physician assessment of disease activity (VAS)
- Patient assessment of disease activity (VAS)
- Patient assessment of pain (VAS)
- Acute phase reactants (CRP / ESR)

For AS patients
- BASDAI
- Physician assesment of disease activity (VAS)
- Patient assesment of disease activity (VAS)
- Patient assessment of pain (VAS)
- Acute phase reactants (CRP / ESR)

- Health related Quality of Life (patient reported outcome) :

For PsA patients
- DLQI
- HAQ - DI

For AS patients
- HAQ-S

- WPAI-SHP (PRO)
- Serious adverse events

6.5.3   Scores and questionnaires used

Disease Activity Score (DAS):

The DAS (37) indicates the severity of the RA. The score varies between 0 and 10, with 10 indicating the highest degree of severity. The DAS is calculated from the following data documented on the physician form:

- Joint status: Number of swollen and tender joints
- ESR (mm/1. h) or CRP (mg/l)
- Patient's assessment of current disease activity (from 0 = inactive to 10 = highly active)

The DAS is calculated by means of a validated algorithm.

BASDAI

BASDAI (32) is a simple, self-reported questionnaire that consists of 6 questions on disease activity. Each is evaluated by a 100 mm horizontal visual analog (VAS) or 0-10 numerical rating scale (NRS). In this study, NRS is preferred. Each NRS is scored from 0 to 10 (0 = no symptoms, 10 = very severe symptoms). The mean of the 2 scores relating to morning stiffness is taken. The resulting 0 to 50 score for the overall index is converted to 0 – 10 scale to give the final BASDAI score. A patient will be considered to have axial disease if BASDAI score is > 4.

Health Assessment Questionnaire (HAQ-DI):

The HAQ (33) is the internationally most-used instrument for assessing RA-related functional impairment. It has been validated in patients with a wide variety of rheumatic diseases. In this study, the short HAQ-DI (Disability Index) is administered. The patient has to answer 20 questions concerning impairment in daily activities within the following 8 areas:

Dressing & Grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, Activities

Patients assess their functionality over the past week by means of a 4-level scale ranging from 0 (without any difficulty) to 3 (unable to do). The highest (worst) values will be calculated into a mean value which indicates the degree of functional impairment (HAQ Disability Index: 0-3). HAQ-DI score is calculated as % in this study.

Health Assessment Questionnaire modified for Spondyloarthropathies (HAQ-S):

The HAQ‑S (35) is a modiefied version of the HAQ questionnaire specific for Spondyloarthropathies, It is a 25‑item scale on which respondents rate the degree of difficulty they have performing tasks in 10 functional areas, with responses ranging from 0 (no difficulty) to 3 (unable to do). The highest (worst) values will be calculated into a mean value which indicates the degree of functional impairment .

Work Productivity and Activity Impairment - Specific Health Problem Questionnaire (WPAI-SHP)

The WPAI (34) is a questionnaire for the self-assessment of work productivity and activity impairment. In this observational study, the WPAI-SHP is used which measures work productivity and activity impairment with reference to a specific health problem. All dimensions relate to the past seven days.

The following dimensions are measured:

- Assessment of employment status
- Assessment of hours missed from work due to health problems and other reasons such as vacation or holidays (total number of hours to be indicated)
- Assessment of hours the patient has actually worked (total number of hours to be indicated)
- Assessment of impairment in work productivity and in regular daily activities (2 assessments with 10 levels each)

The WPAI yields four types of scores:

- 'activity impairment'
- 'absenteeism' (work time missed)
- 'presenteeism' (impairment at work/reduced on-the-job effectiveness) and
- 'work productivity loss' (overall work impairment/absenteeism plus presenteeism).
- Scores are transformed into percentages. Higher scores indicate greater impairment.

Dermatology Life Quality Index (DLQI):

The DLQI (36) is a 10-item, self-administered questionnaire which aims to measure the impact of skin disease on adult patients' quality of life. The following 4 dimensions are measured:

- Skin discomfort
- Self-confidence
- Occupational and leisure activities
- Social interaction

7.0 Adverse Events

7.1 Adverse Event Definition and Serious Adverse Event Categories

An adverse event (AE) is defined as any untoward medical occurrence in a patient, which does not necessarily have a causal relationship with their treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory

finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the labeling, as well as from accidental or intentional overdose, drug abuse, or drug withdrawal. Any worsening of a pre-existing condition or illness is considered an adverse event.

If an adverse event meets any of the following criteria, it is considered a **serious adverse event (SAE)**:

Death of Subject:	An event that results in the death of a subject.
Life-Threatening:	An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.
Hospitalization:	An event that results in an admission to the hospital for any length of time. This does not include an emergency room visit or admission to an outpatient facility.
Prolongation of Hospitalization:	An event that occurs while the study subject is hospitalized and prolongs the subject's hospital stay.
Congenital Anomaly:	An anomaly detected at or after birth, or any anomaly that results in fetal loss.
Persistent or Significant Disability/Incapacity:	An event that results in a condition that substantially interferes with the activities of daily living of a study subject. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may

Serious Outcome:	jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of subject, life threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

7.2   Severity

The physician will use the following definitions to rate the severity for any adverse event being collected as an endpoint/data point in the study and for all serious adverse events.

Mild:	The adverse event is transient and easily tolerated by the subject.
Moderate:	The adverse event causes the subject discomfort and interrupts the subject's usual activities.
Severe:	The adverse event causes considerable interference with the subject's usual activities and may be incapacitating or life threatening.

7.3   Relationship to Pharmaceutical Product

The investigator will use the following definitions to assess the relationship of the adverse event to the use of study drug:

Reasonable Possibility	An adverse event where there is evidence to suggest a causal relationship between the study drug and the adverse event.
No Reasonable Possibility	An adverse event where there is no evidence to suggest a causal relationship between the study drug and the adverse event.

If an investigator's opinion of no reasonable possibility of being related to study drug is given, an alternate etiology must be provided by the investigator for the adverse event.

7.4   Serious Adverse Event Collection Period

Serious adverse events will be reported to AbbVie from the time the physician obtains the patient's authorization to use and disclose information (or the patient's informed consent) until 30 days or 5 half-lives following the intake of the last dose of physician-prescribed treatment.

7.5   Serious Adverse Event Reporting

In the event of a serious adverse event occurring in a patient treated with Humira, whether considered related to Humira or not, the physician will notify the AbbVie contact dentified below by faxing the completed SAE form within 24 hours of the physician becoming aware of the event.

7.6   Pregnancy Reporting

In the event of a pregnancy occurrence in the patient, the physician will notify the AbbVie contact person identified in Section 7.5 within 24 hours of the physician becoming aware of the pregnancy

8.0   Ethics and Quality

Study approval by an Independent Ethics Committee will be obtained before initiating the study. The study will be run according to GCP/ICH guidelines and local regulatory regulations. Each patient will receive appropriate explanation and sign an Informed Consent Form prior to enrollment into the study. Since this study is a post-marketing observational study, a Clinical Trial Authorization from the Competent Authorities is not required.

To ensure data quality the study will be monitored on-site by AbbVie. The case report forms will be reviewed periodically for completeness, legibility and acceptability by AbbVie personnel (or their representatives). AbbVie (or their representatives) will be allowed access to all source documents in order to verify case report form entries. To ensure data quality CRF entries will be verified by the Abbott monitor against source documents for a sample of the patients.

9.0   Case Report Forms

The investigator or staff under his/her supervision will complete case report forms according to the protocol. Only data specified in the protocol should be collected and submitted to AbbVie. All information written on the case report forms will also be reflected in the subject's source documents.

Case report forms will be supplied by AbbVie. These forms will be used to transmit information collected during the study to AbbVie and regulatory authorities, as applicable. Case report forms must be completed for each subject enrolled in this study. All case report forms must be legible and completed in indelible blue or black ballpoint ink. Any necessary corrections are to be made by drawing a single line through the incorrect entry and writing in the revision, and must be initialed and dated by the investigator or his/her representative. Data are not to be obliterated by blacking out, using correction fluid or by

erasing the original entry. If the reason for the correction is not obvious, a brief explanation (*e.g.,* transcription error) should accompany the change. All information written on the case report forms must also be reflected in the subject source documents .

The investigator will review the case report forms for completeness and accuracy and sign and date each set of case report forms where indicated. The case report forms will be reviewed periodically for completeness, legibility and acceptability by AbbVie personnel (or their representatives). AbbVie (or their representatives) will be allowed access to all source documents in order to verify case report form entries.

Once the original case report form has been removed from the site, all changes must be made *via* the appropriate change form specified by AbbVie. The principal investigator will review the change form for completeness and accuracy and sign and date the change form where indicated.

10.0 Data Analysis Plan

The statistical analysis will be performed using SAS software, Version 9.2 or later.

A detailed analysis plan will be developed with the vendor ▮▮▮▮▮▮▮▮▮▮▮▮ before database lock.

10.1 Sample Size

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 (approximately 25) during the foreseen recruitment period of 12 months.

Based on data from Reilly et al (7) 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 from Kimball (9), it is estimated that the standard deviation of the change in TWPI will be about 23.8. Since this estimate is based upon a 16 week treatment period and 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.

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.

10.2 Endpoints

10.2.1 Primary Endpoint

The primary efficacy variable is the change in total work productivity impairment (TWPI) due to AS/PsA between baseline and Month 18.

10.2.2 Secondary Endpoints

- TWPI due to AS at Months 3, 6, 12, and 18
- TWPI due to PsA at Months 3, 6, 12, and 18
- TWPI due to AS or PsA at Months 3, 6, and 12
- Evolution over time of :
  - Number of patients that are employed at each assessed visit
  - Percentage of missed working hours (absenteeism) due to AS/PsA, as measured by TWPI AS/PsA 7 days prior to each visit

- o 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)
- o 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) recorded at each visit
  - o HAQ-S (AS)
  - o HAQ-DI (PsA)
  - o DLQI (PsA)
- Disease activity measures and clinical evaluations recorded at each visit:
  - o BASDAI (AS)
  - o DAS28 (PsA)
  - o BSA (PsA)
  - o Acute phase reactants (CRP / ESR)
  - o Physician assessment of disease activity (VAS)
  - o Patient assessment of disease activity (VAS)
  - o Patient assessment of pain (VAS).

10.3 Statistical Methods

10.3.1 Analysis Sets

The statistical analysis will primarily be based on the Per Protocol analysis set consisting of the patients without major protocol violations. The TWPI-SHP data will also be analyzed on the Intention to Treat set.

10.3.2 Statistical Analysis

The study is essentially descriptive. The numerical variables will be analyzed applying descriptive statistics (mean, 95% confidence interval on the mean, standard deviation, minimum, 1st quartile, median, 3rd quartile, maximum, number of observations). Quantitative variables will be described by means of frequencies and percentages for the

different 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 analysis of the evolution of the work productivity data, the health-related quality of life scores, and the disease activity measures and clinical evaluations will be based upon data collected during time windows around the foreseen routine study visits.

The relationship between disease activity and work status and between clinical evaluations and work status will be evaluated by comparing the onset data for patients currently employed and patients not employed at the baseline visit, and by comparing the data from the 18 month time window for patients currently employed and patients not employed at the corresponding visit.

The relationship between disease activity and work productivity and between clinical evaluations and work productivity will be evaluated on the basis of the correlations with the TWPI for the baseline data.

11.0   Final Report and Publications

Please refer to your investigator site contract for specific information related to publication practices. AbbVie abides by the PhRMA Principles on Conduct of Clinical Trials and Communication of Clinical Trial results. Our registrations and results disclosure adhere to all relevant laws.

12.0 References

1. Braun J, Bollow M, Remlinger G, Eggens U, Rudwaleit M, Distler A, et al. Prevalence of spondyloarthropathies in HLA-B27 positive and negative blood donors. Arthritis Rheum 1998; 41: 58-67.
2. Zink A, Braun J, Listing J, Wollenhaupt J. Disability and handicap in rheumatoid arthritis and ankylosing spondylitis - results from the German rheumatological database. J Rheumatol 2000; 27: 613-22.
3. Barlow JH, Wright CC, Williams B, Keat A. Work disability among people with ankylosing spondylitis. Arthritis Rheum 2001; 45: 424-9.
4. Boonen A, Chorus A, Miedema H, van der Heijde D, van der Tempel H, van der Linden S. Employment, work disability, and work days lost in patients with ankylosing spondylitis: a cross-sectional study of Dutch patients. Ann Rheum Dis 2001; 60: 353-8.
5. Forejtova S, Mann H, Stolfa J, Vedral K, Fenclova I, Nemethova D et al. Factors influencing health status and disability in patients with ankylosing spondylitis in the Czech Republic. Clin Rheumatol 2008; 27: 1005-13.
6. Ward RM; Reveille JD, Learch TJ, Davis JC Jr, Weisman MH. Impact of ankylosing spondylitis on work and family life: comparisons with US population. Arthritis Rheum 2008; 59: 497-503.
7. Ariza-Ariza R, Hernandez-Cruz B, Collantes E, et al. Work disability in patients with ankylosing spondylitis. J Rheumatol 2009; 36: 2512-16.
8. Chorus AM, Boonen A, Miedema HS, et al. Employment perspectives of patients with ankylosing spondylitis. Ann Rheum Dis 2002; 61: 693-9.
9. Boonen A, Chorus A, Miedema A, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. Ann Rheum Dis 2001; 60: 1033-9.
10. Strombeck B, Jacobsson LT, Bremander A, et al. Patients with ankylosing spondylitis have increased sick leave – a registry-based case-control study over 7 years. Rheumatology (Oxford) 2009; 48: 289-92.
11. Barkham N, Kong KO, Tennant A, et al. The unmet need for anti-tumor necrosis factor (anti-TNF) therapy in ankylosing spondylitis. Rheumatology 2005; 44: 1277-81.
12. Boonen A. A review of work-participation, cost-of-illness and cost-effectiveness studies in ankylosing spondylitis. Nat Clin Pract Rheumatol 2006; 2: 546-53.
13. Maksymowych WP. Treatment of ankylosing spondylitis. Rakel and Bope: Conn's Current Therapy, W. B. Saunders Company, 2001; 1021- 3.

14. Wanders A, et al. Nonsteroidal anti-inflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: A randomized clinical trial. Arthritis Rheum 2005; 52: 1756- 65.

15. Heldmann F, Dybowski F, Saracbasi-Zender E, Fendler C, Braun J. Update on biologic therapy in the management of axial spondyloarthritis. Curr Rheumatol Rep 2010; 12: 325-31.

16. van der Heijde D, Kivitz A, Schiff MH, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis. Arthritis Rheum 2006; 54: 2136-46.

17. van der Heijde D, Schiff MH, Sieper J, et al. Adalimumab effectiveness for the treatment of ankylosing spondylitis is maintained for up to 2 years: long-term results from the ATLAS trial. Ann Rheum Dis 2009; 68: 922-9.

18. van der Heijde D, Pangan AL, Schiff MH, et al. Adalimumab effectively reduces the signs and symptoms of active ankylosing spondylitis in patients with total spinal ankylosis. Ann Rheum Dis 2008; 67: 1218-21.

19. Rudwaleit M; Rodevand E, Holck P, et al. Adalimumab effectively reduces the rate of anterior uveitis flares in patients with active ankylosing spondylitis: results of a prospective open-label study. Ann Rheum Dis 2009; 68: 696-701.

20. Davis JC Jr, Revicki D, van der Heijde DMF, et al. Health-related quality of life outcomes in patients with active ankylosing spondylitis treated with adalimumab: results from a randomized controlled study. Arthritis Rheum 2007; 57: 1050-7.

21. Maksymowych WP, Gooch KL, Wong RL, et al. Impact of age, sex, physical function, health-related quality of life, and treatment with adalimumab on work status and work productivity of patients with ankylosing spondylitis. J Rheumatol 2010; 37: 385-92.

22. Boumpas DT, Illei GG, Tassiulas IO. Psoriatic arthritis. In: Klippel JH, Crofford LJ, Stone JH, Weyand CM, editors. Primer on the Rheumatic Diseases. Edition 12. Georgia: Arthritis Foundation, 2002: 233-238.

23. Gladman DD. Psoriatic arthritis: Recent advances in pathogenesis and treatment. Rheum Dis Clin North Am 1992;18(1):247-56.

24. Verstappen SMM, Watson KD, Lunt M et al. On behalf of the BSR Biologics Register. Rheumatology 2010; 49: 1570-77.

25. Wallenius M, Skomsvoll JF, Koldingsnes W et al. Work disability and health-related quality of life in males and females with psoriatic arthritis. Ann Rheum Dis 2009; 68: 685-9.

26. Goupille P. Which second line treatments are optimal in psoriatic arthritis? Joint Bone Spine 2002;69:244-248.

27. Poddubnyy DA, Rudwaleit DA. Adalimumab for the treatment of psoriatic arthritis. Expert Rev Clin Immunol 2009; 5: 671-81.

28. Gladman DD, Mease PJ, Cifaldi MA et al. Adalimumab improves joint-related and skin-related functional impairment in patients with psoriatic arthritis: patient-reported outcomes of the Adalimumab Effectiveness in Psoriatic Arthritis Trial. Ann Rheum Dis 2007: 66: 163-8.

29. Barra L, Pope JE, Payne M. Real-world anti-tumor necrosis factor treatment in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: cost-effectiveness based on number needed to treat to improve health assessment questionnaire. J Rheumatol 2009; 36: 1421-8.

30. Kavanaugh A, Antoni C, Mease P et al. Effect of infliximab therapy on employment, time lost from work, and productivity in patients with psoriatic arthritis. J Rheumatol 2006; 33: 2254-9.

31. Gladman DD for the ACCLAIM Study Investigators: Responses to adalimumab in patients with active psoriatic arthritis who have not adequately responded to prior therapy: effectiveness and safety results from an open-label study. J Rheumatol 2010: 37: 1898-906.

32. Garrett S, Jenkinson T, Kennedy LG et al.. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994; 21: 2286-91.

33. Buchbinder R et al. Which outcome measures should be used in rheumatoid arthritis clinical trials? Clinical and quality-of-life measures' responsiveness to treatment in a randomized controlled trial. Arthritis Rheum 1995; 38:1568–80.

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

35. Daltroy LH, Larson MG, Roberts NW, Liang MH. A modification of the Health Assessment Questionnaire for the spondyloarthropathies. J Rheumatol. 1990;17(7):946-50

36. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): A simple practical measure for routine clinical use. Clinical and Experimental Dermatology 1994; 19: 210-216

37. Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44–8.

13.0　　　　Appendices

APPENDIX A: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Please tick the box which represents your answer to each question. All questions refer to last week.

1. How would you describe the overall level of fatigue/tiredness you have experienced?

NONE ⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧ VERY SEVERE
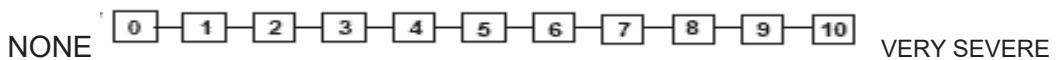
2. How would you describe the overall level of AS neck, back or hip pain you have had?

NONE ⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧ VERY SEVERE
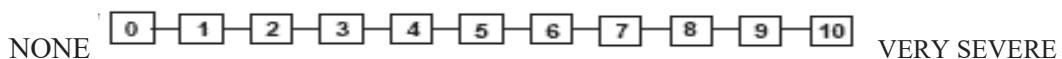
3. How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?

NONE ⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧ VERY SEVERE
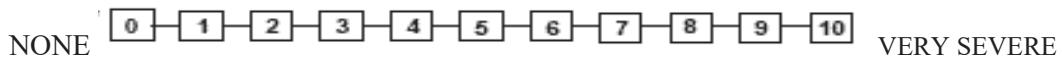
4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?

NONE ⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧ VERY SEVERE
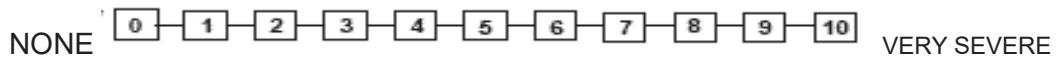
5. How would you describe the overall level of morning stiffness you have had from the time you wake up?

NONE ⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧ VERY SEVERE
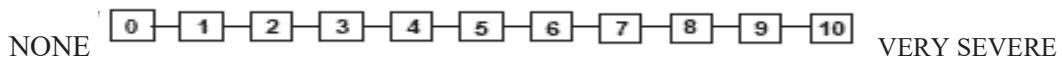
6. How long does your morning stiffness last from the time you wake up?

⟦0⟧—⟦1⟧—⟦2⟧—⟦3⟧—⟦4⟧—⟦5⟧—⟦6⟧—⟦7⟧—⟦8⟧—⟦9⟧—⟦10⟧

0 h　　　　　　　　1 h　　　　　　　2 or more h

Adalimumab
P13-990
FINAL 06 December 2012
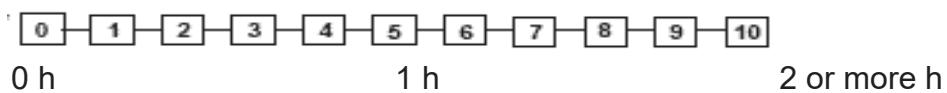
Scoring of the BASDAI:
The BASDAI Score has a maximum value of 10.
Translate the time from question 6 into a number from 0-10 (e.g. ¼ h = 1,25; ½ h = 2,5; ¾ h = 3,75 etc)
BASDAI Score = 0,2 x (Item 1 + Item 2 + Item 3 + Item 4 + $\underline{\text{Item 5}}$ + $\underline{\text{Item 6}}$)
$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad$ 2 $\qquad$ 2

BASDAI score: ....(0-10)

APPENDIX B: Disease Activity Index/ 28 joints (DAS 28)

1. Tender Joints	2. Swollen Joints
☐ No ☐ Yes	☐ No ☐ Yes
If yes, the TOTAL number of tender joints:	If yes, the TOTAL number of swollen joints:

3. ESR (mm/1^{rst} hr): ☐☐☐
(Erythrocyte Sedimentation Rate)

4. Patient's global assessment of disease activity (0-100 mm VAS):
Considering all the ways in which the arthritis may affect your patient at this time, please ask him/her the following question:

How active is the disease at the moment?

INACTIVE (0)   HIGHLY ACTIVE (100)

Formula for calculation of DAS28 ESR:

$$DAS28_{ESR} = 0.56 \times \sqrt{TJ} + 0.28 \times \sqrt{SJ} + 0.70 \times \ln(ESR\ 1^{st}\ hour) + 0.014 \times Patients\ global\ assessment\ of\ disease$$

DAS 28 score: ....

APPENDIX C: Health Assessment Questionnaire Disability Index (HAQ-DI)

In this section we are interested in learning how your illness affects your ability to function in daily life.

Please tick the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do

DRESSING & GROOMING
Are you able to:
- Dress yourself, including tying shoelaces and doing up buttons?
- Wash your hair?

RISING
Are you able to:

- Stand up from a straight chair?
- Get in and out of bed?

EATING
Are you able to:
- Cut up your meat?
- Lift a full cup or glass to your mouth?
- Open a new milk carton ?

WALKING
Are you able to:
- Walk outdoors on flat ground?
- Climb up five steps?

Please tick the response which best describes your usual abilities **OVER THE PAST WEEK**:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do

HYGIENE

Are you able to:
- Wash and dry your body?
- Have a bath?
- Get on and off the toilet?

REACH

Are you able to:
- Reach up for and take down a 5 lb object (e.g.: a bag of potatoes) from just above your head?
- Bend down to pick up clothing from the floor?

GRIP

Are you able to:
- Open car doors?
- Open jars which have been previously opened?
- Turn taps on and off?

ACTIVITIES

Are you able to:
- Go shopping?
- Get in and out of a car?
- Do chores such as vacuuming and gardening?

APPENDIX D: Work Productivity and Activity Impairment - Specific Health Problem Questionnaire (WPAI-SHP)

The following questions ask about the effect of your **DISEASE (Ankylosing Spondylitis = AS or Psoriatic Arthritis = PsA)** on your ability to work and perform regular activities. *Please fill in the blanks or circle a number, as indicated.*

1. Are you currently employed (working for pay)? _____ NO ___ YES
     If NO, check "NO" and skip to question 6.

The next questions are about the **past seven days**, not including today:

2. During the past seven days, how many hours did you miss from work because of <u>problems associated with your AS or PsA</u>? *Include hours you missed on sick days, times you went in late, left early, etc., because of your AS or PsA:*

    _____ HOURS

3. During the past seven days, how many hours did you miss from work because of <u>any other reason</u>, such as vacation, or holidays?

    _____HOURS

4. During the past seven days, how many hours did you actually work?

    _____HOURS *(If "0", skip to question 6.)*

5. During the past seven days, how much did your AS or PsA affect your productivity <u>while you were working</u>?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If AS or PsA affected your work only a little, choose a low number. Choose a high number if AS or PsA affected your work a great deal.

Consider only how much AS or PsA affected productivity <u>while you were working</u>.

| AS or PsA had no effect on my work | 0 1 2 3 4 5 6 7 8 9 10 | AS or PsA completely prevented me from working |

CIRCLE A NUMBER
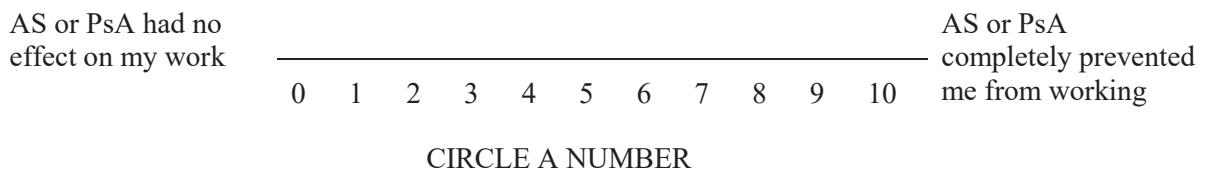
6. During the past seven days, how much did your AS or PsA affect your ability to do your regular daily activities, other than work at a job? *By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If AS or PsA affected your activities only a little, choose a low number. Choose a high number if AS or PsA affected your activities a great deal.*

Consider only how much AS or PsA affected your ability to do your regular daily activities, other than work at a job.
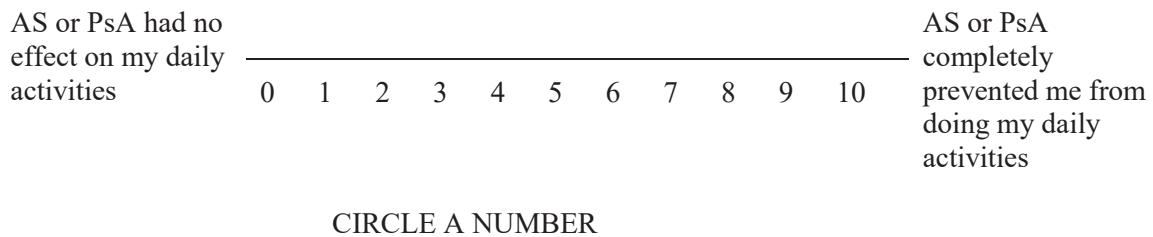
| AS or PsA had no effect on my daily activities | 0 1 2 3 4 5 6 7 8 9 10 | AS or PsA completely prevented me from doing my daily activities |

CIRCLE A NUMBER

APPENDIX E: Dermatology Life Quality Index (DLQI)

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard?**	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □

7.	Over the last week, has your skin prevented you from **working** or **studying**?	yes	□	
		no	□	Not relevant □
	If "No," over the last week how much has your skin been a problem at **work** or **studying**?	A lot	□	
		A little	□	
		Not at all	□	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much	□	
		A lot	□	
		A little	□	
		Not at all	□	Not relevant □

Please check you have answered EVERY question. Thank you.

© AY Finlay, GK Khan, April 1992

APPENDIX F: Health Assessment Questionnaire modified for Spondyloarthropathies (HAQ-S)

HEALTH ASSESSMENT QUESTIONNAIRE MODIFIED FOR THE SPONDYLOARTHROPATHIES (HAQ-S) 1 OF 3

Modified Health Assessment Questionnaire for Spondyloarthropathies (HAQ-S)

Place an "x" in the box which best describes your abilities OVER THE PAST WEEK:

	WITHOUT ANY DIFFICULTY	WITH SOME DIFFICULTY	WITH MUCH DIFFICULTY	UNABLE TO DO
DRESSING AND GROOMING Are you able to:				
Dress yourself, including shoelaces and buttons?	☐ 0	☐ 1	☐ 2	☐ 3
Shampoo your hair?	☐ 0	☐ 1	☐ 2	☐ 3
ARISING Are you able to:				
Stand up from a straight chair?	☐ 0	☐ 1	☐ 2	☐ 3
Get in and out of bed?	☐ 0	☐ 1	☐ 2	☐ 3
EATING Are you able to:				
Cut your own meat?	☐ 0	☐ 1	☐ 2	☐ 3
Lift a full cup or glass to your mouth?	☐ 0	☐ 1	☐ 2	☐ 3
Open a new milk carton?	☐ 0	☐ 1	☐ 2	☐ 3
WALKING Are you able to:				
Walk outdoors on a flat ground?	☐ 0	☐ 1	☐ 2	☐ 3
Climb up five steps?	☐ 0	☐ 1	☐ 2	☐ 3

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

☐ Devices used for dressing (button hook, zipper pull etc.)   ☐ Built up or special utensils   ☐ Crutches
☐ Special or built up chair   ☐ Cane   ☐ Wheelchair
☐ Walker

Daltroy LH, Larson MG, Roberts NW, Liang MH. A modification of the Health Assessment Questionnaire for the spondyloarthropathies. J Rheumatol. 1990;17(7):946-50.

Are y

Daltroy l
J Rheun

Adalimumab
P13-990
FINAL 06 December 2012

Adalimumab
P13-990
FINAL 06 December 2012

APPENDIX G: Study Plan

	Screening	Baseline	Month 3	Month 6	Month 12	Month 18 (or term.)
Informed Consent	♦					
Inclusion/ Exclusion Criteria	♦					
Medical History		♦				
Demographics (gender, year of birth, race)		♦				
AS & PSA diagnosis		♦				
Previous and current AS&PsA treatments		♦				
Extra articular disease manifestations		♦	♦	♦	♦	♦
Educational background		♦				
Employment situation		♦	♦	♦	♦	♦
Disease activity measures and clinical evaluations : DAS28*, BSA*, physician assessment disease activity, acute phase reactants (CRP/ESR), BASDAI**, patient assessment of disease activity, patient assessment of pain		♦	♦	♦	♦	♦
Healt related quality of life (DLQI*, HAQ-DI*, HAQ-S**)		♦	♦	♦	♦	♦
WPAI-SHP		♦	♦	♦	♦	♦
Serious Adverse Events		♦	♦	♦	♦	♦

Screening and basline assessments can happen in the same visit

Follow up visits are according to daily clinicla practice, no additional visits are planned for the study only.

*only completed for PsA patients

** only completed for AS patients

APPENDIX H: Informed Consent Form

**Observational study in Ankylosing Spondylitis and Psoriatic Arthritis patients
to evaluate work productivity before and after the start of Humira therapy
in daily practice in Belgium**

SPACTIVE Study.

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

For updated version of the informed consent, please see ICF section of the Investigator Site File

---

APPENDIX I: Investigator's Agreement

1. I have read this protocol and agree to its content.

2. I agree to conduct the study as outlined in the protocol and in accordance with all applicable regulations and guidelines.

3. I agree to maintain the confidentiality of all information received or developed in connection with the protocol.

_____   _____

Signature of Principal Investigator   Date

AbbVie

Clinical Study Protocol (P13-990)

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

<u>Approved by:</u>