STATISTICAL ANALYSIS PLAN
STUDY W15-679 (STRIKE)

Version *1.0*

03 April 2018

General Information

Protocol	STRIKE – Treating Patients with Early Axial Spondyloarthritis to Target – a 1 Year Randomized Controlled Study Taking an Intense Treatment Approach Versus Routine Treatment - W15-679
Document definition	Statistical Analysis Plan (SAP) – Version 1.*0.* 03 April 2018
Related Documents	Study Protocol, dated 30 March 2017
Document owner	IST GmbH, Soldnerstrasse 1, D-68219 Mannheim

TABLE OF CONTENTS Page

GLOSSARY OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine aminostransferase
AS	Ankylosing Spondylitis
ASAS	Assessment of Spondyloarthritis International Society
ASAS HI	Assessment of Spondyloarthritis International Society Health Index
AST	Aspartate aminostransferase
axSpA	Axial Spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMIlin	Linear Bath Ankylosing Spondylitis Metrology Index
CI	Confidence Interval
CD74 CLIP	Cluster of Differentiation 74 Class II-associated Invariant Chain Peptide
CRF	Case Report Form
CRP	C-reactive Protein
eCRF	Electronic Case Report Form
EQ-5D	European Quality of Life – 5 Dimension Questionnaire
ESR	Erythrocyte Sedimentation Rate
HBc Ab	Hepatitis B core antibody
HBs Ab	Hepatitis B surface antibody
HBs Ag	Hepatitis B Surface Antigen
HBV	Hepatitis B virus
HI	Health Index
HIV	Human Immunodeficiency Virus
HLA-B27	Human Leukocyte Antigen-B27
HPF	High-power field
ITT	Intent to Treat
MASES	Maastricht Ankylosing Spondylitis Enthesitis Score
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging

GLOSSARY OF ABBREVIATIONS

NA	Not Available
ND	Not Done
NRS	Numerical Rating Scale
NSAID	Nonsteroidal Anti-inflammatory Drug
PCR	Polymerase chain reaction
PP	Per-protocol
RA	Rheumatoid Arthritis
RBC	Red Blood Cell
SI	Sacroiliac
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SI	Système International d'Unités
SOC	Standard of Care
SpA	Spondyloarthritis
T2T	Treat to Target
TAI	Total Activity Impairment
TB	Tuberculosis
TNF	Tumor Necrosis Factor
TNFα	Tumor Necrosis Factor Alpha
TWP	Total Work Productivity Impairment
ULN	Upper Limit of Normal
WBC	White Blood Cell
WPAI-axSpA	Work Productivity and Activity Impairment – axSpA

1. INTRODUCTION

There is an unmet medical need for the treatment of axial spondyloarthritis (axSpA). In this study, a 'treat to target' (T2T) treatment scheme escalating to combination treatment with one nonsteroidal anti-inflammatory drug (NSAID) and adalimumab (if needed) is investigated.

According to the ASAS and European League Against Rheumatism (EULAR) recommendations, NSAIDs are the first line of therapy in symptomatic patients with axSpA. Tumor necrosis factor alpha (TNFα)-blocking agents (TNF-blockers) are recommended in active axSpA with predominant axial manifestations if patients are still active after starting an NSAID therapy or if there are contraindication for an NSAID therapy. However, conventional DMARDs are not effective for the treatment the axial component of spondyloarthritis (SpA). In case of peripheral arthritis and/or enthesitis local glucocorticosteroid injections can be considered. Currently NSAIDs and TNF-blockers are the only effective and approved drugs for the treatment of axSpA.

Adalimumab (the TNF-blocker used in this study) was first approved for the treatment of subjects with rheumatoid arthritis (RA) in the United States (US) in December 2002 and in the European Union (EU) in September 2003. Adalimumab therapy has a well-established and well described safety profile based on extensive post-marketing experience and continued clinical trial patient exposure since the first approved indication in 2002 for rheumatoid arthritis.

Recently, similar to previous T2T recommendations for RA, T2T recommendations for the whole group of SpA including patients with axSpA and psoriatic arthritis have been developed. However, axSpA treatment targets and treatment escalation strategies have not been identified and validated in a prospective study.

Therefore, in this study an intensified T2T treatment approach comprising clearly defined treatment targets and cut-offs for treatment escalation shall be investigated in comparison to standard of care (SOC) treatment.

2. STUDY OBJECTIVES

The objectives of this study are:

Primary objective:

The primary objective of this study is to compare a T2T intense treatment approach with a routine treatment approach (SOC) in reducing disease activity at Week 32 in patients with axSpA.

Secondary objectives are to compare a T2T intense treatment approach with SOC by assessing the following at Week 32 and Week 52:

Improvement of quality of life

- Quality of life by the European Quality of Life – 5 Dimension Questionnaire (EQ-5D)
- Overall functioning by Assessment of Spondyloarthritis International Society (ASAS) Health Index (HI)

Improvement of function

- Function – Represented by the Bath Ankylosing Spondylitis (AS) Functional Index (BASFI) Numerical Rating Scale (NRS) score (0 to 10)

Improvement of work productivity

- Work Productivity and Activity Impairment – Axial Spondyloarthritis (WPAI-axSpA)

Reducing inflammation

- Active inflammation as measured by magnetic resonance imaging of the sacroiliac joints and the spine (Berlin Magnetic Resonance Imaging [MRI] scores for the sacroiliac [SI] joints and spine)
- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR)

Reducing disease activity

- Disease activity as measured by Bath AS Disease Activity Index (BASDAI)
- Percentage of subjects achieving 50% improvement in BASDAI (BASDAI 50 response)
- Change from Baseline in disease activity measured by Ankylosing Spondylitis Disease Activity Score (ASDAS)
- Percentage of subjects achieving ASDAS major improvement
- Percentage of subjects achieving ASDAS clinically important improvement
- Percentage of subjects in ASDAS inactive disease (ASDAS < 1.3)
- Percentage of subjects with low disease activity (ASDAS < 2.1)
- Percentage of subjects with moderate disease activity (ASDAS ≥ 1.3 to < 2.1)
- Percentage of subjects with high disease activity (ASDAS ≥ 2.1 to < 3.5)
- Percentage of subjects with very high disease activity (ASDAS ≥ 3.5)
- Percentage of subjects achieving ASAS 20, ASAS 40, and ASAS Partial Remission
- Change from Baseline in Physician's Global Assessment of Disease Activity
- Change from Baseline in Patient's Global Assessment of Disease Activity
- Change from Baseline in Patient's Global Assessment of Pain
- Change from Baseline in Swollen Joint Count (66 joints)
- Change from Baseline in Tender Joint Count (68 joints)
- Change from Baseline in the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)
- Change from Baseline in the Dactylitis count (0 – 20)

- Change from Baseline in Linear Bath Ankylosing Spondylitis Metrology Index (BASMIlin)
- Anterior uveitis

Other variables to be analyzed at various time points including Week 32 and Week 52:

- ASDAS course over time
- BASDAI course over time

Exploratory Objectives:

- Serum autoantibodies against cluster of differentiation 74 class II-associated invariant chain peptide (CD74 CLIP)
- Reduction of disease progression (as measured by MRI of the sacroiliac joints and the spine)

3. STUDY DESIGN

3.1 Overview of Study Design and Dosing Regimen

This is a Phase 4, multicenter, randomized, open-label, parallel-group study comparing an intensified T2T treatment approach with SOC.
The study duration will include a 42-day Screening period, a 52-week treatment period (treatment T2T according to randomization or SOC), and – only for subjects who receive study drug Humira (adalimumab) but do not continue on commercially available Humira after the study – a 70 day follow-up phone call.
Subjects who have signed the informed consent and who fulfill all screening criteria will be randomized 1:1 to receive either treatment following an intensified T2T approach (T2T group) or treatment according to SOC (following the local practice standards) (SOC group). Study drug will only be administered to patients of the T2T group escalated to Escalation Step 2. Length of exposure will depend on individual necessity for intensifying treatment. The maximal duration of treatment with adalimumab is up to 48 weeks.

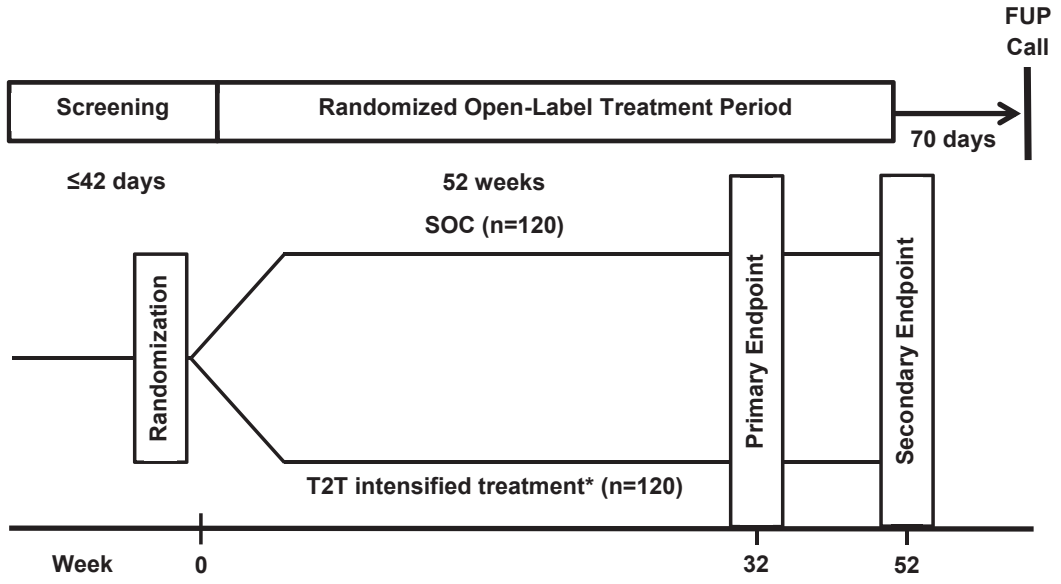
<u>T2T Group (Investigational Group):</u>
After randomization subjects are seen at Weeks 2, 4, 6, 8 and afterwards every 4 weeks up to Week 52.
Basic treatment will be started with a non-steroidal anti-inflammatory drug (NSAID). Treatment should be intensified (escalated) beginning at Week 4 if the ASDAS is $\geq$ 2.1 (escalation step 1). Treatment escalation is planned to be initiated at Week 4, if needed and further escalation is planned at Week 8, if needed (escalation step 2). However, if not required at Week 8, treatment can be escalated at every visit thereafter if the ongoing treatment is not sufficiently efficacious and the escalation step 2 has not yet been reached. Treatment escalation steps are as follows:

- Basic treatment (NSAID 1): Treatment will be started with any NSAID and given for 4 weeks at full anti-inflammatory dose. If at Week 2 ASAS 20 response is not achieved, subjects may escape early to Escalation Step 1. If the chosen NSAID cannot be continued due to intolerance, escalation to the next escalation step is possible at any time point. If basic treatment is well tolerated and sufficiently efficacious the subject will be continued on this treatment.

- Escalation step 1 (NSAID 2): Treatment will be changed to a second NSAID if after 4 weeks of treatment the first NSAID is not sufficiently efficacious (ASDAS ≥ 2.1) and/or not tolerated. The second NSAID will be given for 4 weeks. Early escape is possible if after 2 weeks no ASAS 20 response is achieved. In this case treatment can be switched to escalation step 2 after 2 weeks of NSAID 2. If the chosen NSAID cannot be continued due to intolerance, escalation to the next escalation step is possible at any time point. If NSAID 2 treatment is well tolerated and sufficiently efficacious the subject will be continued on this treatment.
- Escalation step 2 (Combination with adalimumab): In case of failure of NSAID 2 (ASDAS ≥ 2.1 after 4 weeks of NSAID 2) the treatment will be intensified by switching to the combination of NSAID and adalimumab 40 mg s.c. every other week (eow). Escalation step 2 can be initiated at Week 4 visit at the earliest if early escape is chosen during Basic Treatment and during NSAID 2.

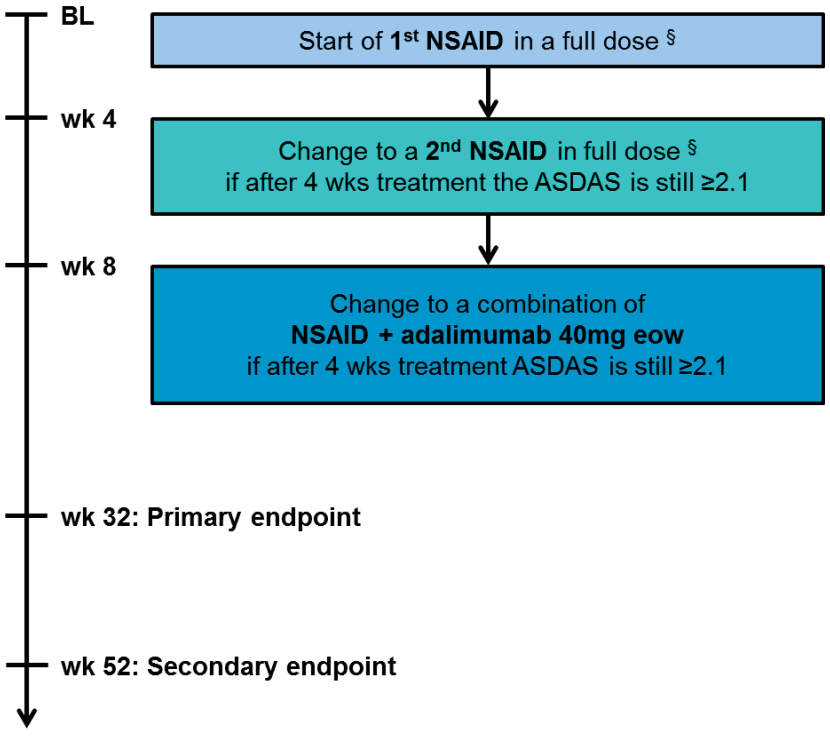
SOC Group (Reference Group):
After randomization, subjects will receive treatment according to local practice standards. Subjects are seen at Weeks 12, 24, 32, and 52.

Figure 1. Study Design Schematic



* Escalation schedule for the T2T intensified treatment see below.

Escalation in the T2T intensified treatment group



§ Early escape after 2 wks NSAIDs intake: In case of no ASAS 20 response or intolerance switch to next escalation step (2nd NSAID/NSAID+ADA)

3.2 Sample Size Calculation

Based on available data from previous studies it is assumed that ASDAS inactive disease could be reached by 40% in the T2T group versus 20% in the control group. In total 2 × 90 evaluable subjects are necessary to detect with 80% power an increase in ASDAS inactive disease at Week 32 from 20% in the SOC arm to 40% in the intensified T2T arm, if a two sided Fisher's exact test is applied. If the Pearson chi-square test instead of the Fisher's exact test can be applied, then only 2 × 83 subjects are necessary.
Assuming that about 18% of the randomized subjects will drop out prior to Week 32 and have to be counted as non-responder the assumed ASDAS inactive disease rate will be diluted to 16.4% in the SOC arm and 32.8% in the intensified T2T arm. The necessary sample size for this scenario (intent to treat [ITT] population) is 2 × 109 subjects for the chi-square test and 2 × 119 subjects for the Fisher's exact test. In summary, 2 × 120 subjects should be randomized.

4. STATISTICAL CONSIDERATIONS AND ANALYTICAL PLAN

4.1 Primary and Secondary Efficacy Parameters

4.1.1 Primary Efficacy Parameter

The primary efficacy parameter is the clinical disease activity at Week 32 measured by the ASDAS.

The ASDAS is defined as follows:

$ASDAS_{CRP}$ = 0.12 × total back pain [BASDAI question 2] + 0.110 × global disease activity [Patient global assessment of disease activity] + 0.07 × peripheral pain/swelling [BASDAI question 3] + 0.06 × duration of morning stiffness [BASDAI question 6] + 0.58 × ln(CRP [in mg/L]+1)

$ASDAS_{ESR}$ (Alternative) = 0.08 × total back pain [BASDAI question 2] + 0.110 × global disease activity [Patient global assessment of disease activity] + 0.09 × peripheral pain/swelling [BASDAI question 3] + 0.07 × duration of morning stiffness [BASDAI question 6] + 0.29 × √ESR [in mm/hr]

Inactive disease is defined as ASDAS < 1.3. Low disease activity is defined as ASDAS < 2.1, moderate disease activity as ASDAS ≥ 1.3 to < 2.1, high disease activity as ASDAS ≥ 2.1 to ≤ 3.5, and very high disease activity as ASDAS >3.5. [3-7]

To follow ASAS, the evaluation of total back pain will be changed from patient's assessment of total back pain (as described in the Protocol) to result of BASDAI question 2.

No imputation will be performed for missing items, and in case of missing items no index score will be calculated.

4.1.2 Secondary Efficacy Parameters

Secondary efficacy parameters are:

Quality of life by the European Quality of Life (EQ-5D)

The EQ-5D-3L is a health state utility instrument that evaluates preference for health status (utility). The 5 items in the EQ-5D-3L comprise 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each of which are rated on 3 levels of severity (1: indicating no problem, 2: indicating some/moderate problems, 3: indicating extreme problems), and a separate VAS.

Patients' responses to the EQ-5D-3L will be combined into a unique health state using a 5-digit code with one digit from each of the 5 dimensions representing the level of severity. These EQ-5D-3L states will be converted into a single preference-weighted health utility index score by applying country-specific weights. [1]

No imputation will be performed for missing items, and in case of missing items no index score will be calculated.

Work Productivity and Activity Impairment – axSpA (WPAI-axSpA)

The WPAI questionnaire will be used to measure work absenteeism, work presenteeism, and daily activity impairment. The WPAI-axSpA V2.0 is the axSpA specific questionnaire that will be used in this study. The WPAI-axSpA consists of 6 questions (Q1-Q6). Respondents are asked about time missed from work and time while at work during which productivity was impaired in the past seven days. Results of WPAI are expressed as a percentage of impairment from 0 to 100, with higher percentages indicating greater impairment and less productivity:

- % Presenteeism – percentage of impairment while working due to health problem: 100*Q5/10
- % Absenteeism – percentage of work time missed due to health problem: 100*Q2/(Q2+Q4)
- % Total work productivity impairment (TWP) – percentage of overall work impairment due to health problem: 100*{Q2/(Q2+Q4) + [Q4/(Q2+Q4)]* Q5/10}
- % Total activity impairment (TAI) – percentage of general (non-work) activity impairment due to health problem: 100*Q6/10

The four scores will be derived according to the WPAI-SHP scoring manual [2] using the following coding rules for contradictory or missing information:

- If employed = YES or employed = NO or missing and hours missed or worked > 0, then employed. If employed = missing and hours missed and worked = 0, then not employed.
- If hours worked = 0, then productivity while at work is not applicable.
- A score will be set to missing if one or more of the items Q1-6 that are needed for the calculation of the score are missing. No imputation will be performed for missing items.

- Someone who missed all work hours due to health is 100% impaired.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

The subject will assess his/her disease activity in answering 6 questions pertaining to symptoms experienced by the subject during the past week on a numerical rating scales (NRS, 0 = None to 10 severe or 0= 0h to 5 = 1h to 10 = 2 or more h). The score is defined as follows:

BASDAI Score = 0.2 x (Item 1 + Item 2 + Item 3 + Item 4 + 0.5 x Item 5+ 0.5 x Item 6)

A major clinical response will be defined as a 50% improvement or more of the initial BASDAI (BASDAI 50). [8, 9]No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Bath Ankylosing Spondylitis Functional Index (BASFI)

The subject will assess his/her ability of ten selected activities for the past week using a NRS (0= easy to 10=Impossible). The BASFI is the mean of these 10 item scores.[8]

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Linear Bath Ankylosing Spondylitis Metrology Index ($BASMI_{lin}$)

The BASMI will be conducted at the designated study visits to evaluate spinal mobility in a subject. The five assessments are scored as follows:

- Lateral lumbar flexion (mean right/left) (21.1 cm - RESULT)/2.1 cm
- Tragus to wall distance (mean right/left) (RESULT - 8 cm)/3 cm
- Lumbar flexion (modified Schober) (7.4 cm - RESULT)/0.7 cm
- Maximal intermalleolar distance (124.5 cm - RESULT)/10 cm
- Cervical rotation angle (mean right/left) (89.3° - RESULT)/8.5°

The mean score of the five assessments gives the BASMI linear result (0-10). [8]

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Magnetic Resonance Imaging (MRI) of the Spine and Sacroiliac Joints

All subjects will have a MRI evaluation of the sacroiliac (SI) joints as well as the cervical, thoracic and lumbar regions of the spine at screening and the last visit (at week 52 visit or – in case of early discontinuation – the discontinuation visit). Images will be sent to the central imaging vendor designated by the Sponsor. Images will be scored for inflammatory lesions and chronic structural changes in the spine and the sacroiliac joints using a modified version of the Berlin MRI score. [11] For this purpose, each SI joint will be divided into four quadrants and the

spine into 23 vertebral units which will be rated according to Table 1. Summing up the gradings yields the following scores:

- Sacroiliac joints
    - Active inflammation (0-24)
    - Erosion (0-24)
    - Fatty deposition (0-24)
    - Sclerosis (0-2)
    - Ankylosis (0-2)
- Spine
    - Active Inflammation (0-69)
    - Erosion (0-23)
    - Fatty deposition (0-69)
    - Bone proliferation (0-69)
    - Activity in facet joints (0-23)
    - Activity in Proc. spinosus (0-23)
    - Activity of soft tissue in posterior spinal sites (0-23)

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Table 1 Berlin Magnetic Resonance Imaging (MRI) Score for the Spine and the Sacroiliac Joints

	Grade 0	Grade 1	Grade 2	Grade 3
Sacroiliac joints				
Active inflammation (BMO of quadrant area)	Absent	Up to 33% of the quadrant area	33% – 66%	> 66%
Erosions (per quadrant)	Absent	Minor (one to two erosions)	Moderate (three to five single erosions	Multiple (confluent erosions)
Fatty bone marrow deposition (per quadrant)	Absent	< 33%	33-– 66%	>66%
Sclerosis (per joint)	Absent	Present	--	--
Ankylosis (per joint)	Absent	Present	--	--
Spine				
Active Inflammation (BMO of VU area)	Absent	< 33% of VU area	33% – 66%	> 66%
Erosions (% of the bone surface per VU)	Absent	present		
Fatty bone marrow deposition (per VU)	Absent	< 33%	33% – 66%	> 66%
Bone proliferation (per VU)	Absent	Syndesmophytes without bridging	Bridging syndesmophytes	Transdiscal ankylosis
Activity in facet joints (right and/or left)	Absent	present		--
Activity in Proc. spinosus	Absent	present		
Activity of soft tissue in posterior spinal sites	Absent	present		

BMO = bone marrow edema; VU = vertebral unit

Assessment of Disease Activity and Pain

NRSs will be used to assess:

- Physician's global assessment of disease activity
- Patient's global assessment of disease activity
- Patient's global assessment of pain
- Patient's assessment of nocturnal back pain within the last week
- Patient's assessment of total back pain within the last week.

The left end of the NRS (0) signifies the absence of symptoms and the right end (10) signifies maximum activity or pain.

Assessment of Spondyloarthritis International Society (ASAS) Health Index (HI)

The ASAS HI will assess the overall functioning of each subject. The responses to the 17 dichotomous items can be summed up to give a total score ranging from 0 to 17 - with a lower score indicating a better and a higher score indicating an inferior health status.[10]

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

ASAS 20, ASAS 40, and ASAS Partial Remission

The ASAS response criteria are defined as follows [6]:

- ASAS20 response: improvement of ≥ 20% and absolute improvement of ≥ 1 unit (on a scale of 0 to 10) from Baseline in ≥ 3 of the following 4 domains, with no deterioration in the remaining domain (defined as a worsening of ≥ 20% and a net worsening of ≥ 1 unit)
    - Patient's Global Assessment – Represented by the PTGA-disease activity NRS score (0 to 10)
    - Pain – Represented by the patient's assessment of total back pain NRS score (0 to 10)
    - Function – Represented by the BASFI NRS score (0 to 10)
    - Inflammation – Represented by the mean of the 2 morning stiffness-related BASDAI NRS scores (mean of items 5 and 6 of the BASDAI [0 to 10])
- ASAS40 response: improvement of ≥ 40% and absolute improvement of ≥ 2 units (on a scale of 0 to 10) from Baseline in ≥ 3 of the 4 domains above in ASAS20 with no deterioration at all in the potential remaining domain
- ASAS partial remission: absolute score of ≤ 2 units for each of the 4 domains identified above in ASAS20

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)

At the designated study visits the presence or absence of enthesitis at 13 different sites will be assessed. All sites are scored as 0 (absent) or 1 (present). The MASES is the sum of all site scores (from 0 to 13). [8]

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Swollen and tender joint counts

An assessment of 68 joints will be done by physical examination at the designated study visits. The joints will be examined for tenderness (score: 0-68) and swelling (score: 0-66). The joints to be examined for swelling are the same as those examined for tenderness, except the hip joints are excluded. Enthesitis is not part of the swollen joint assessment.

No imputation will be performed for missing items, and in case of missing items or joint replacements no score will be calculated.

Dactylitis counts

Evaluation for dactlyitis will be conducted at the designated study visits to assess the presence or absence of dactylitis in all 20 of the subjects' digits (score: 0-20).

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Anterior uveitis

At the screening visit a detailed medical history of anterior uveitis, as confirmed by an ophthalmologist, will be documented. At baseline and all subsequent visits, new onsets of uveitis (right, left or both) and/or the number of flares since last visit will be documented.

No imputation will be performed for missing items, and in case of missing items no score will be calculated.

Laboratory parameters - exploratory and efficacy analyses

The following laboratory parameters will be assessed: C-reactive protein (CRP [mg/L]) and erythrocyte sedimentation rate (ESR [mm/h (1st hour)]). Exploratory analysis of CD74CLIP will not be performed.

For further details on the assessment of serum autoantibodies against CD74 CLIP, CRP and ESR please refer to Section 4.2.5.3.

4.2 Statistical and Analytical Methods

4.2.1 Analysis Populations

Subjects are screened to ensure they meet all inclusion criteria and none of the exclusion criteria mentioned below at both Screening and Baseline Visits.

Main Inclusion:

1. Subjects must have signed written informed consent before starting any study-related assessments or procedures.
2. Diagnosis of axSpA (either ankylosing spondylitis or non-radiographic axSpA) and fulfilling the ASAS classification criteria for axSpA.
3. Subjects aged ≥ 18 years.
4. Disease duration < 5 years.
5. Subjects must have a baseline disease activity as defined by having an ASDAS ≥ 2.1 or a BASDAI ≥ 4.
6. Subjects must be either NSAID-naïve or had not been treated with the maximal recommended dose during the last 2 weeks prior to the Baseline Visit.
7. Subjects must be disease-modifying anti-rheumatic drug (DMARD)-naïve except for methotrexate (MTX), sulfasalazine (SSZ), azathioprine (AZA), and 6-mercaptopurine (6-MP).
8. Subjects must never have failed a NSAID taken at maximal recommended dose for 2 weeks or more.
9. If female, subject must be either postmenopausal, OR permanently surgically sterile OR for Women of Childbearing Potential practicing at least one protocol specified method of birth control, starting at Study Day 1 through at least 150 days after the last dose of study drug.

   If the male subject is sexually active with female partner(s) of childbearing potential, he must agree, from Study Day 1 through 20 weeks after the last dose of study drug, to practice the protocol specified contraception.
10. Females of childbearing potential must have a negative serum pregnancy test result at Screening, and a negative urine pregnancy test at Baseline Visit.

    Females of non-childbearing potential (either postmenopausal or permanently surgically sterile as defined above) at Screening do not require pregnancy testing.
11. Subject is judged to be in good health as determined by the Principal Investigator based upon the results of medical history, laboratory profile, physical examination, and a 12-lead ECG performed at Screening.
12. Subjects must be able and willing to self-administer SC injections or have a qualified person available to administer SC injections.

13. Subjects must be able and willing to provide written informed consent and comply with the requirements of this study protocol.

Main Exclusion:

1. Contraindications for NSAIDs or Tumor Necrosis Factor (TNF) blocker according to local labeling.
2. Subject has a medical condition precluding an MRI (e.g., magnetic activated implanted devices – cardiac pace-maker, insulin pump, neurostimulators, etc. and metallic devices or fragments in the body).
3. Subject has active inflammatory bowel disease.
4. Prior exposure to any anti-TNF therapy; any biologic therapy with a potential therapeutic impact on SpA, or subject has been treated with any investigational drug of chemical or biologic nature within a minimum of 30 days or five half-lives (whichever is longer) of the drug prior to the Baseline Visit.
5. If entering the study on concomitant NSAIDs, subjects taking the maximal recommended dose during the last 2 weeks prior to the Baseline Visit or have failed or developed intolerance to a NSAID taken at maximal recommended dose for 2 weeks or more at any time.
6. Subject on opioid analgesics or use of marijuana within 14 days prior to the Baseline Visit.
7. If entering the study on concomitant oral corticosteroids, subject has not been on stable dose of prednisone (≤ 10 mg per day), or oral corticosteroid equivalents, for at least 14 days prior to the Baseline Visit.
8. Subject has been treated with intra-articular joint injection(s) or spinal/paraspinal injection(s) of corticosteroids in the preceding 28 days prior to the Baseline Visit.
9. Subject has undergone spinal surgery within 2 months prior to Baseline or subject has been diagnosed with a spinal condition that may interfere with study assessments (i.e., disc herniation, degenerative spine disease, etc.) in the opinion of the investigator.
10. Subject has a history of fibromyalgia or inflammatory arthritis of a different etiology other than SpA (e.g., rheumatoid arthritis, systemic lupus erythematosus, polyarticular or systemic juvenile idiopathic arthritis).
11. Infection(s) requiring treatment with intravenous (IV) anti-infectives within 30 days prior to the Baseline Visit or oral anti-infectives within 14 days prior to the Baseline Visit.
12. Known hypersensitivity to adalimumab or its excipients as stated in the label.
13. Known intolerance of NSAID treatment that does not allow use of at least two different NSAIDs at full anti-inflammatory dose.
14. History of demyelinating disease (including myelitis) or neurologic symptoms suggestive of demyelinating disease.

15. History of invasive infection (e.g., listeriosis and histoplasmosis), human immunodeficiency virus (HIV).
16. Subjects with any active viral infection that based on the investigator's clinical assessment, makes the subject an unsuitable candidate for the study.
17. Hepatitis B: Hepatitis B surface antigen (HBs Ag) positive (+) or detected sensitivity on the hepatitis B virus (HBV)-DNA polymerase chain reaction (PCR) qualitative test for hepatitis B core antibody (HBc Ab)/hepatitis B surface antibody (HBs Ab) positive subjects.
18. Chronic recurring infections or active TB.
19. History of moderate to severe congestive heart failure (New York Heart Association [NYHA] class III or IV), recent cerebrovascular accident and any other condition which would put the subject at risk by participation in the study.
20. Evidence of dysplasia or history of malignancy (including lymphoma and leukemia) other than a successfully treated non-metastatic cutaneous squamous cell, basal cell carcinoma or localized carcinoma in situ of the cervix.
21. Positive pregnancy test at Screening or Baseline.
22. Female subject who is pregnant, breastfeeding or is considering becoming pregnant during the study or for approximately 150 days after the last dose of study drug.
23. Male subject who is considering fathering a child or donating sperm during the study or for approximately 150 days after the last dose of study drug.
24. Clinically significant abnormal screening laboratory results as evaluated by the Investigator.
25. History of clinically significant drug or alcohol abuse in the last 12 months.
26. Subject is considered by the Investigator, for any reason, to be an unsuitable candidate for the study.
27. Any vulnerable subject (e.g., person kept in detention, or dependent from the Sponsor, Investigator or study site)

Enrolled population is defined as all patients who signed written informed consent.

Intent-to-treat analysis (ITT) population is defined as all patients enrolled who were randomized.

Safety analysis (SP) population is defined all patients enrolled who were randomized and received treatment for axSpA after randomization.

Per-protocol (PP) population is defined as all patients of the ITT population who have sufficient data regarding the primary efficacy endpoint (clinical disease activity at Week 32) and did not meet any major protocol violation.

4.2.2 Definition of Baseline and Visit Time Windows

For each subject, study day 1 is defined as the day of randomization. For baseline analyses the last available value prior to or on the day of randomization will be used.

Subjects are allowed a visit window of ± 7 days for all study visits (after baseline).

If a subject has an out of window visit, the next visit should occur as originally scheduled based on the date of the baseline visit.

In subjects of the T2T group, HBV screening, TB screening and chest X-ray (CXR) will be performed before Escalation Step 2 is initiated (before adalimumab is administered).

If a subject is diagnosed with latent TB the subject has to undergo a minimum of 1 month of anti-TB prophylaxis before Escalation Step 2 can be initiated. In this case the time until the next visit will be counted from the start of adalimumab; e.g., if a subject starts TB prophylaxis at Week 8 visit and initiates Escalation Step 2 after receiving 2 months of prophylaxis, i.e., 16 weeks after Baseline, the next visit (nominal Week 12 visit) will be postponed by these 2 months (to 20 weeks after Baseline). All subsequent visits will be postponed accordingly, e.g., Week 16 visit to 24 weeks after Baseline.

If a subject is diagnosed with active hepatitis B the subject is not eligible to receive adalimumab and should discontinue from the study.

4.2.3 Patient Disposition

The absolute and relative numbers of the patients enrolled [rescreened patients are only counted once], the patients in the ITT and the patients in the SP will be displayed. The number of patients in the PP will not be displayed because the study was stopped prematurely by the sponsor. However, the number of patients of the SP who are treated for axSpA after randomization but meet at least one major protocol violation will be displayed, including the major protocol violations. Major protocol violations will be identified by an expert with the help of data listings. (See also section 4.2.8) Multiple violations could be reported per patient.

Furthermore the absolute and relative numbers of the patients completing the treatment phase and the reason why not by frequency (i.e. termination of study by sponsor, adverse event(s), failure to return, pregnancy, insufficient therapeutic response, withdrawn consent, death, other [including specifications will be displayed last]) will be displayed. Multiple reasons could be reported per patient.

Information about patient disposition will be listed as well.

An overview of tables and listings is given in Table 2.

4.2.4 Baseline Characteristics

Demographic and baseline characteristics will be summarized for SP in total and by treatment groups. The number of observations, mean, standard deviation, median, quartiles, minimum and maximum will be summarized for continuous variables. Discrete variables will be summarized via counts and percentages.

All baseline characteristics will be listed. An overview of listings and tables is given in Table 2.

4.2.4.1 Demographic Characteristics

The following demographic characteristics will be summarized:

- Sex (Male, Female)
- Age at randomization [years], flooring the difference between date of randomization and date of birth divided by 365.25 [The year of birth is reported only, so the date of will be completed via 30th June.]
- Height [cm]
- Weight [kg]
- BMI [kg/sqm]

The last value up to and including study day 1 will be displayed.

4.2.4.2 Medical and Surgical History

The following variables will be summarized:

- History of Tuberculosis (TB)
    - Past TB infection (Yes, No, Unknown)
    - High TB risk (Yes, No)
    - Former BCG vaccination (Yes, No, Unknown)
- Medical History for axSpA
    - Uveitis (Never, Former, Current, Unknown)
    - Inflammatory bowel disease (Never, Former, Current, Unknown)
    - Psoriasis (Never, Former, Current, Unknown)
    - Other features of spondyloarthritis (Inflammatory back pain, Arthritis (past), Heel enthesitis (past), Good prior response to NSAIDs, Family history of SpA)
- Surgical History for axSpA
    - History of spinal surgery for axSpA (Yes, No)
    - History of joint replacement for axSpA (Yes, No)
    - History of surgery for axSpA (Yes, No)
    - History of arthroscopy for axSpA (Yes, No)
    - Other medical history (Yes, No)

The last value up to and including study day 1 will be displayed.

4.2.4.3 Laboratory Data

The following clinical chemistry and hematology laboratory parameters will be summarized:

- Creatinine [micromol/L]
- Total bilirubin [micromol/L]
- Albumin [g/L]
- Aspartate aminostransferase [AST in U/L]
- Alanine aminostransferase [ALT in U/L]
- Glucose [mmol/L]
- Hematocrit [ratio]
- Hemoglobin [g/L]
- Red Blood Cell Count [RBC in 10**12/L]
- White Blood Cell Count [WBC in 10**9/L]
- Neutrophils [10**9/L]
- Bands [10**9/L]
- Lymphocytes [10**9/L]
- Monocytes [10**9/L]
- Basophils [10**9/L]
- Eosinophils [10**9/L]
- Platelets [10**9/L]

The following parameters of macroscopic urinalysis will be summarized:

- Specific Gravity (1.005, 1.010, 1.015, 1.020, 1.025, 1.030, NA/ND)
- Ketones (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Protein (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Glucose (Negative, Trace, +, ++, +++, ++++, NA/ND)
- pH (4.5, 5, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, NA/ND)
- Nitrite (Negative, Positive, NA/ND)
- Blood (Negative, Trace, +, ++, +++, ++++, NA/ND)

The following parameters of microscopic urinalysis will be summarized:

- Leucocytes [number / HPF]
- Erythrocytes [number / HPF]
- Dysmorphic erythrocytes [number / HPF]
- Epithelial cells [number / HPF]
- Bacteria [number / HPF]
- Yeasts [number / HPF]
- Casts [number / HPF]
- Crystal [number / HPF]

Microscopic Urinalysis is performed if the dipstic results of macroscopic urinalysis show protein, ketones or blood greater than negative or glucose greater than normal.

The following other parameters will be summarized:

- ESR [mm/h (1st hour)]
- CRP [mg/L]
- Anti-dsDNA Antibodies (Negative, Positive)
- HLA-B27 (Negative, Positive)
- HBsAg (Negative, Positive)
- HBsAb (Negative, Positive) in patients with HBsAg negative
- HBcAb (Negative, Positive) in patients with HBsAg negative
- HBV DNA PCR (Below detection sensitivity, Meeting/exceeding detection sensitivity) in patients with HBsAg negative, HBsAb negative, and HBcAb Total positive

The last value up to and including study day 1 will be displayed. For conversion factors see 4.2.6.3.

4.2.4.4 Prior medication

Treatments, surgical and medical procedures will be coded by AbbVie assigning appropriate preferred terms. The absolute and relative numbers of patients taking prior drug for axSpA and other prior drugs will be displayed. The drugs will be displayed via preferred term.

The medication started prior to study day 1 will be displayed.

4.2.5 Analyses of Efficacy

All variables will be listed. An overview of listings, figures and tables is given in Table 2.

4.2.5.1 Primary Variable

ASDAS will be plotted over time by subject and treatment group for the SP. The limits 1.3, 2.1 and 3.5 will be displayed as well. No non-responder imputation or LOCF will be applied and no statistical tests and no sensitivity analysis will be performed because the study was terminated prematurely by the sponsor.

4.2.5.2 Secondary Variables

All secondary variables, except for CD74 CLIP (see below) will be listed only, since the study was terminated prematurely by the sponsor.

4.2.5.3 Exploratory Analyses

No exploratory analyses will be performed because the study was terminated prematurely by the sponsor. CD74 CLIP will not be presented as readouts have not been performed. However, data on CRP and ESR, as well as data of the MRIs, will be presented as part of the Safety Analysis, see Section 4.2.6.

4.2.5.4 Subgroup Analyses

No subgroup analyses will be performed.

4.2.6 Analyses of Safety

All variables will be listed. An overview of listings, figures and tables is given in Table 2.

4.2.6.1 Exposure to Study Medication

All medications taken will be listed only because the study was terminated prematurely by the sponsor.

4.2.6.2 Adverse Events

Adverse events (AEs) are coded by IST GmbH. A treatment-emergent adverse event is defined as AE that starts either on or after randomization or is related to study treatment. AEs will be displayed for the SP in total and by treatment group.

An overview of the number of patients with at least one of the following AEs is given:

- AE
- Malignancy, i.e. AEs fulfilling criteria for malignancy and the patient is <=30 years at time of onset of AE
- Serious AEs (SAEs)
- Life-threatening AEs
- AEs leading to death

- AEs leading to hospitalization
- Important medical event requiring medical or surgical intervention to prevent serious outcome
- AEs leading to persistent or significant disability/incapacity
- AEs leading to congenital anomalies
- AEs possibly related to HUMIRA
- AEs leading to withdrawal of HUMIRA
- AEs leading to interruption of HUMIRA
- AEs leading to start of co-medication or therapy
- AEs leading to discontinuation of co-medication or therapy
- AEs leading to study discontinuation

Furthermore, treatment-emergent AEs will be summarized via system organ class (SOC) and preferred term once overall and once by severity.

In addition, non-serious AEs will be summarized. Here, only preferred terms are taken into account that occurred at a frequency of >=5% in any treatment group.

Serious AEs, AEs leading to death, AEs leading to hospitalization, AEs possibly related to HUMIRA, AEs leading to permanent withdrawal from HUMIRA, and AEs leading to interruption of HUMIRA intake will be listed only.

4.2.6.3 Laboratory Data

The following clinical hematology laboratory parameters will be plotted over time by subject and treatment group for the SP:

- Hematocrit [ratio]
- Hemoglobin [g/L]
- Red Blood Cell Count [RBC in [10**12/L]]
- White Blood Cell Count [WBC in [10**9/L]]
- Neutrophils [10**9/L]
- Bands [10**9/L]
- Lymphocytes [10**9/L]
- Monocytes [10**9/L]
- Basophils [10**9/L]
- Eosinophils [10**9/L]
- Platelets [10**9/L]

The following clinical chemistry laboratory parameters will be plotted over time by subject and treatment group for the SP:

- Creatinine [micromol/L]
- Total Bilirubin [micromol/L]
- Total Bilirubin / ULN
- Albumin [g/L]
- AST [U/L]
- AST / ULN
- ALT [U/L]
- ALT / ULN
- Glucose [mmol/L]

Furthermore, ESR [mm/h (1st hour)] and CRP [mg/L] will be plotted over time by subject and treatment group for the SP.

The following parameters of microscopic urinalysis will be plotted over time by subject and treatment group for the SP:

- Leucocytes [number / HPF]
- Erythrocytes [number / HPF]
- Dysmorphic erythrocytes [number / HPF]
- Epithelial cells [number / HPF]
- Bacteria [number / HPF]
- Yeasts [number / HPF]
- Casts [number / HPF]
- Crystal [number / HPF]

Microscopic Urinalysis is performed if the dipstic results of macroscopic urinalysis show protein, ketones or blood greater than negative or glucose greater than normal.

Absolute and relative number of patients over time will be displayed for parameters of macroscopic urinalysis and other laboratory parameters. The last value up to and including the relevant visit (as defined in section 4.2.2) will be displayed.

The following parameters of macroscopic urinalysis will be summarized:

- Specific Gravity (1.005, 1.010, 1.015, 1.020, 1.025, 1.030, NA/ND)
- Ketones (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Protein (Negative, Trace, +, ++, +++, ++++, NA/ND)

- Glucose (Negative, Trace, +, ++, +++, ++++, NA/ND)
- pH (4.5, 5, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, NA/ND)
- Nitrite (Negative, Positive, NA/ND)
- Blood (Negative, Trace, +, ++, +++, ++++, NA/ND)

The following conversion factors will be used:

Parameter	In	To	Conversion factor
Hematocrit	%	ratio	0.01
Hemoglobin	mmol/L	g/L	64.5
Creatinine	mg/L mg/dL	micromol/L	8.84 88.4
Total Bilirubin	mg/dL	micromol/L	17.1
Albumin	g/dL	g/L	10
AST	microkat/L	U/L	59.88
ALT	microkat/L	U/L	59.88
Glucose	mg/dL g/L	mmol/L	0.0555 5.55
CRP	mg/dL	mg/L	10

4.2.6.4 Vital Signs

The following parameters will be plotted over time by subject and treatment group for the SP:

- Systolic blood pressure [mmHg]
- Diastolic blood pressure [mmHg]
- Pulse [bpm]
- Respiratory rate [breath per minute]
- Body temperature [°C]
- BMI [kg/sqm]

4.2.6.5 Co-medication

Treatments, surgical and medical procedures will be coded by AbbVie assigning appropriate preferred terms. Concomitant medications are defined as all medication except medication for axSpA received after day one. The absolute and relative numbers of patients taking co-medications will be displayed for SP overall and by treatment group. The drugs will be displayed via preferred term.

Table 2 Overview of Outputs

Output Title	Output Short Name	Analysis Population
Tables and figures		
Patient Disposition by Treatment Group - EP	tdis_t_ep	Enrolled population
Reasons for Premature Termination of the Treatment Phase by Treatment group - SP	tps_t_SP	Safety population
Demographic Characteristics by Treatment Group – SP	tdm_t_sp	Safety population
Medical and Surgical History at Baseline by Treatment Group – SP	tmsh_t_sp	Safety population
Chemistry and Hematology Laboratory Variables at Baseline by Treatment Group – SP	tchl_t_sp	Safety population
Macroscopic Urinalysis Laboratory Variables at Baseline by Treatment Group – SP	tmaul_t_sp	Safety population
Microscopic Urinalysis Laboratory Variables at Baseline by Treatment Group – SP	tmiul_t_sp	Safety population
Other Laboratory Variables at Baseline by Treatment Group – SP	totl_t_sp	Safety population
Prior Medication by Treatment Group - SP	tpm_t_sp	Safety population
Ankylosing Spondylitis Disease Activity Score ($ASDAS_{CRP}$) by Treatment Group - SP	fasdascrp_t_sp	Safety population
Ankylosing Spondylitis Disease Activity Score ($ASDAS_{ESR}$) by Treatment Group - SP	fasdasesr_t_sp	Safety population
Overview of Treatment-emergent Adverse Events by Treatment Group - SP	toae_t_sp	Safety population
Treatment-emergent Adverse Events by Treatment Group - SP	tae_t_sp	Safety population
Treatment-emergent Adverse Events by Severity and Treatment Group - SP	taes_t_sp	Safety population
Treatment-emergent Non-serious Adverse Events by Treatment Group - SP	tnsae_t_sp	Safety population
Laboratory Hematology by Treatment Group – SP	flh_tc_sp	Safety population

Output Title	Output Short Name	Analysis Population
Laboratory Clinical Chemistry by Treatment Group – SP	flc_t_sp	Safety population
Laboratory Microscopic Urinalysis by Treatment Group – SP	flmu_t_sp	Safety population
Vital Signs by Treatment Group - SP	fvs_t_sp	Safety population
Laboratory Macroscopic Urinalysis by Treatment Group – SP	tlmu_t_s	Safety population
Other Laboratory Tests by Treatment Group - SP	flo_t_s	Safety population
Concomitant Medication by Treatment Group - SP	tcmd_t_sp	Safety population
Glossary of System Organ Class, MedDRA Preferred Terms and Verbatim Terms for Adverse Events or Diseases	tgae	-
Glossary of Preferred Terms and Verbatim Terms for Concomitant Medication	tgcom	-
Listings		
Patient Disposition	ldis_en	Enrolled population
Inclusion and Exclusion Criteria	lie_en	Enrolled population
Baseline Demographic Characteristics	ldm_en	Enrolled population
Medical and Surgical History: Tobacco or Alcohol Use	ltau_en	Enrolled population
Medical and Surgical History: Axial Spondyloarthritis and Other History	lhao_en	Enrolled population
Prior Medication for axSpA	lpma_en	Enrolled population
All Other Prior Medication	lopm_en	Enrolled population
Treatment Exposure	lte_en	Enrolled population

Output Title	**Output Short Name**	**Analysis Population**
Concomitant Medication	lcom_en	Enrolled population
Adverse Events	lae_en	Enrolled population
Malignancy	lmae_en	Enrolled population
Serious Adverse Events	lsae_en	Enrolled population
Adverse Events Leading to Death	laed_en	Enrolled population
Adverse Events Leading to Hospitalization	laeh_en	Enrolled population
Adverse Events Possibly Related to HUMIRA	laer_en	Enrolled population
Adverse Events Leading to Permanent Withdrawal from HUMIRA	laew_en	Enrolled population
Adverse Events Leading to Interruption of HUMIRA Intake	laei_en	Enrolled population
Pregnancy Test	lpt_en	Enrolled population
Laboratory Clinical Chemistry	llc_en	Enrolled population
Laboratory Hematology	llh_en	Enrolled population
Microscopic Urinalysis	lmiu_en	Enrolled population
Macroscopic Urinalysis	lmau_en	Enrolled population
ESR/CRP	lec_en	Enrolled population
Hepatitis B Testing	lhb_en	Enrolled population
Vital Signs/ Weight	lvs_en	Enrolled population
Dactylitis	lda_en	Enrolled population
Anterior Uveitis	lau_en	Enrolled population
Physical Examinations	lpe_en	Enrolled population

Output Title	Output Short Name	Analysis Population
ECG	lecg_en	Enrolled population
Tuberculosis	ltb_en	Enrolled population
Chest X-Ray	lxr_en	Enrolled population
Ankylosing Spondylitis Disease Activity Score (ASDAS)	lasd_en	Enrolled population
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)	lbas_en	Enrolled population
Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)	lmas_en	Enrolled population
ASAS Health Index (HI)	lahi_en	Enrolled population
ASAS20, ASAS40 and ASAS Partial remission	lrc_en	Enrolled population
Bath Ankylosing Spondylitis Functional Index (BASFI)	lbasfi_en	Enrolled population
Bath Ankylosing Spondylitis Metrology Index (BASMI lin)	lbasmi_en	Enrolled population
EQ-5D	lq_en	Enrolled population
WPAI-axSpA	lwp_en	Enrolled population
Physician's/Patient's Assessment, NRS	lpa_en	Enrolled population
Baseline MRI with Investigator Assessments	lmribl_en	Enrolled population
Berlin MRI Score for MRI of Sacroiliac Joint	lbj_en	Enrolled population
Berlin MRI Score for MRI of Spine	lbs_en	Enrolled population
Tender and Swollen Joints	lts_en	Enrolled population

The layouts of the tables mentioned above are provided in Part II of the SAP (Table Shells).

4.2.7 Interim Analyses

No interim analysis is planned for this study.

4.2.8 Protocol Violations and Deviations

AbbVie does not allow intentional/prospective deviations from the protocol. The Principal Investigator is responsible for complying with all protocol requirements, and applicable global and local laws regarding protocol deviations. If a protocol deviation occurs (or is identified) after a subject has been enrolled, the Principal Investigator is responsible for notifying IEC/IRB regulatory authorities (as applicable), and their assigned CRO Clinical Monitor or the responsible AbbVie Clinical Monitors.

Such contact must be made as soon as possible to permit a review by AbbVie to determine the impact of the deviation on the subject and/or the study.

For the purposes of this protocol, reportable deviations are defined as:

- Subject entered into the study even though she/he did not satisfy entry criteria
- Subject who developed withdrawal criteria during the study and was not withdrawn
- Subject who received wrong treatment or incorrect dose
- Subject who received excluded or prohibited concomitant treatment

A subject may withdraw from the study at any time. The investigator may discontinue any subject's participation prematurely for any reason, including an adverse event, safety concerns or failure to comply with the protocol.

5. DATA QUALITY ASSURANCE

Computer logic and manual checks will be created to identify items such as inconsistent study dates. Any necessary corrections will be made to the eCRF.

An Investigator's Meeting will be held with AbbVie personnel, the investigators and their study coordinators and the Monitors for the study. This meeting will include a detailed discussion of the scientific rational, protocol, performance of study procedures, eCRF and Subject Diary and log completion, Imaging requirement, and specimen collection methods. In addition to or instead of the Investigator's Meeting, the study personnel at each site may be trained on the study procedures by a Monitor at a study initiation visit and will be given an eCRF completion guideline for reference.

The CRO Monitors will monitor each site throughout the study. Source document review will be performed against entries in the eCRF database and a quality assurance check will be performed to ensure that the investigator is complying with the protocol and regulations.

All central laboratory results will be electronically transferred from the central laboratory to the study database.

A review of the data will be conducted by a physician and clinical review team at AbbVie as specified in the safety review plan.

All statistical programs employed in the analysis and reporting of the data will be validated according the standard operating procedures of IST and results will be checked for plausibility.

6. METHODS OF DATA ANALYSIS AND PRESENTATION

All statistical analyses will be carried out by means of the SAS® package (Version 9.4).

6.1 Analysis Data Sets

A value added dataset STRATIFY will be programmed. This will contain derived variables, e.g. analysis populations, treatment regimen and relevant baseline characteristics, needed for the generation of the planned analyses.

A value added dataset AE will be programmed. This will contain all information regarding AEs including preferred term and SOC.

A value added dataset LAB will be programmed. This will contain all information regarding laboratory test results including converted results.

Additional value added dataset will be programmed for the primary and secondary endpoints.

6.2 SAS Output Format

Detailed descriptions of the SAS outputs are given in Part II of the SAP (Table Shells).

7. REFERENCES

1. EQ-5D-3L User Guide; Basic information on how to use the EQ-5D-3L instrument. Prepared by Mandy van Reenen / Mark Oppe. Version 5.1; April 2015
2. Reilly Associates: WPAI Scoring. http://www.reillyassociates.net/WPAI_Scoring.html. 17.09.2015
3. Machado P, Navarro-Compan V, Landewé R, et al.: Calculating the Ankylosing Spondylitis Disease Activity Score If the Conventional C-Reactive Protein Level Is Below the Limit of Detection or If High-Sensitivity C-Reactive Protein Is Used: An Analysis in the DESIR Cohort. Arthritis Rheumatol. 2015 Feb;67(2):408-13.
4. Machado P, Landewe R, Lie E, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. Ann Rheum Dis. 2011;70(1):47-53.
5. Lukas C, Landewé R, Sieper J, et al; Assessment of SpondyloArthritis international Society. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:18-24.
6. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis International Society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis. 2009;68;ii1-ii44.
7. van der Heijde D, Lie E, Kvien TK, Sieper J, van den Bosch F, Listing J, Braun J, Landewé R. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:1811-8.
8. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis. 2009;68;ii1-ii44. doi:10.1136/ard.2008.104018.
9. Rudwaleit M, Listing J, Brandt J, Braun J, Sieper J. Prediction of a major clinical response (BASDAI 50) to tumour necrosis factor alpha blockers in ankylosing spondylitis. Ann Rheum Dis. 2004;63(6):665-70.
10. Kiltz U, van der Heijde D, Boonen A, et al. Development of a health index in patients with ankylosing spondylitis (ASAS HI): final result of a global initiative based on the ICF guided by ASAS. Ann Rheum Dis. 2015;74:830-835.
11. Althoff CE, Sieper J, Song IH, et al. Active inflammation and structural change in early active axial spondyloarthritis as detected by whole-body MRI. Ann Rheum Dis. 2013;72:967-73.

Statistical Analysis Plan
Part II
TABLE SHELLS

Protocol W15-679 (STRIKE)

Version 1.*0*

03 April 2018

Table of Contents Page

List of Tables

Page

List of Figures

Page

List of Listings **Page**

1. TEMPLATES FOR PATIENT DISPOSITIONS

Table 1 Patient Disposition by Treatment Group - EP

tdis_t_ep: Patient Disposition by Treatment Group - EP
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population – Data Extract: <DATE>

	T2T (N=)		SOC (N=)		Not Randomized (N=)		Total (N=)	
Enrolled (EP)	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Number of patients randomized (ITT)	xxx	(xxx.x)	xxx	(xxx.x)			xxx	(xxx.x)
Number of patients who received treatment for axSpA after randomization (SP)	xxx	(xxx.x)	xxx	(xxx.x)			xxx	(xxx.x)
Number of patients of the SP who received treatment for axSpA after randomization but met at least one major protocol violation*	xxx	(xxx.x)	xxx	(xxx.x)			xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)			xxx	(xxx.x)
xxx								

Percentages are based on the number of patients in the relevant population. * Multiple violations could be reported per patient.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Table 2 Reasons for Premature Termination of the Treatment Phase by Treatment group - SP

tps_t_SP: Reasons for Premature Termination of the Treatment Phase by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract: <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Treatment phase completion						
Yes	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
No	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Missing	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
n	xxx		xxx		xxx	
Reasons for not completing treatment phase**						
Early terminiation of study by sponsor	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Adverse event(s)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Death	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Failure to return	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Pregnancy	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Insufficient Therapeutic Response	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Withdrawn consent	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Other	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
XXX	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Missing	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
n	xxx		xxx	(	xxx	

Percentages are based on n. **In patients who did not complete treatment. Multiple reasons could be reported per patient.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

2. TEMPLATES FOR BASELINE CHARACTERISTICS

Table 3 Demographic Characteristics by Treatment Group – SP

tdm_t_sp: Demographic Characteristics by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population - Data Extract <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Sex						
Male	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Female	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Missing	xxx		xxx		xxx	
n	xxx		xxx		xxx	
Age at randomization [years]						
Mean	xxx		xxx		xxx	
SD	xxx		xxx		xxx	
Median	xxx		xxx		xxx	
Q1-Q3	xxx	-xxx	xxx	-xxx	xxx	-xxx
Min-Max	xxx	-xxx	xxx	-xxx	xxx	-xxx
Missing	xxx		xxx		xxx	
n	xxx		xxx		xxx	
Height [cm]						
Mean	xxx		xxx		xxx	
SD	xxx		xxx		xxx	
Median	xxx		xxx		xxx	
Min-Max	xxx	-xxx	xxx	-xxx	xxx	-xxx
Q1-Q3	xxx	-xxx	xxx	-xxx	xxx	-xxx
Min-Max	xxx		xxx		xxx	
n	xxx		xxx		xxx	

n represents number of patients contributing to summary statistics.
Percentages are based on n (number of valid values).

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

tdm_t_sp: Demographic Characteristics by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Weight [kg]						
Mean	xxx		xxx		xxx	
SD	xxx		xxx		xxx	
Median	xxx		xxx		xxx	
Q1-Q3	xxx	-xxx	xxx	-xxx	xxx	-xxx
Min-Max	xxx	-xxx	xxx	-xxx	xxx	-xxx
Missing	xxx		xxx		xxx	
n	xxx		xxx		xxx	
BMI [kg/sqm]						
Mean	xxx		xxx		xxx	
SD	xxx		xxx		xxx	
Median	xxx		xxx		xxx	
Q1-Q3	xxx	-xxx	xxx	-xxx	xxx	-xxx
Min-Max	xxx	-xxx	xxx	-xxx	xxx	-xxx
Missing	xxx		xxx		xxx	
n	xxx		xxx		xxx	

n represents number of patients contributing to summary statistics.
Percentages are based on n (number of valid values).

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

[Last value ≤ day of randomization will be displayed.]

Table 4 Medical and Surgical History at Baseline by Treatment Group – SP

```
tmsh_t_sp: Medical history for axSpA at Baseline by Treatment Group  - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population - Data Extract <DATE>
```

The same layout as in Table 3 will be used. The following variables will be displayed:

History of TB

- Past TB infection (Yes, No, Unknown)
- High TB risk (Yes, No)
- Former BCG Vaccination (Yes, No, Unknown)

Medical History for axSpA

- Uveitis (Never, Former, Current, Unknown)
- Inflammatory bowel disease (Never, Former, Current, Unknown)
- Psoriasis (Never, Former, Current, Unknown)
- Other features of Spondyloarthritis (Inflammatory back pain, Arthritis (past), Heel enthesitis (past), Good prior response to NSAIDs, Family history of SpA)

Surgical History for axSpA

- History of spinal surgery for axSpA (Yes, No)
- History of joint replacement for axSpA (Yes, No)
- History of surgery for axSpA (Yes, No)
- History of arthroscopy for axSpA (Yes, No)
- Other Medical History (Yes, No)

```
[Last value ≤ day of randomization will be displayed.]
```

Table 5 Chemistry and Hematology Laboratory Variables at Baseline by Treatment Group – SP

```
tchl_t_sp: Chemistry and Hematology Laboratory Data at Baseline by Treatment Group  - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population - Data Extract <DATE>
```

The same layout as in Table 3 will be used. The following variables will be displayed:

- Creatinine [micromol/L]
- Total bilirubin [micromol/L]
- Albumin [g/L]
- Aspartate aminostransferase [AST in U/L]
- Alanine aminostransferase [ALT in U/L]
- Glucose [mmol/L]
- Hematocrit [ratio]
- Hemoglobin [g/L]
- Red Blood Cell Count [RBC in [10**12/L]]
- White Blood Cell Count [WBC in [10**9/L]]
- Neutrophils [10**9/L]
- Bands [10**9/L]
- Lymphocytes [10**9/L]
- Monocytes [10**9/L]
- Basophils [10**9/L]
- Eosinophils [10**9/L]
- Platelets [10**9/L]

[Last value ≤ day of randomization will be displayed.]

Table 6 Macroscopic Urinalysis Laboratory Variables at Baseline by Treatment Group – SP

tmaul_t_sp: Macroscopic Urinalysis Laboratory Data at Baseline by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract <DATE>

The same layout as in Table 3 will be used. The following variables will be displayed:

- Specific Gravity (1.005, 1.010, 1.015, 1.020, 1.025, 1.030, NA/ND)
- Ketones (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Protein (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Glucose (Negative, Trace, +, ++, +++, ++++, NA/ND)
- pH (4.5, 5, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, NA/ND)
- Nitrite (Negative, Positive, NA/ND)
- Blood (Negative, Trace, +, ++, +++, ++++, NA/ND)

[Last value ≤ day of randomization will be displayed.]

Table 7 Microscopic Urinalysis Laboratory Variables at Baseline by Treatment Group – SP

tmiul_t_sp: Microscopic Urinalysis Laboratory Data at Baseline by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract <DATE>

The same layout as in Table 3 will be used. The following variables will be displayed (If the dipstic results show protein, ketones or blood greater than negative or glucose greater than normal)

- Leucocytes [number / HPF]
- Erythrocytes [number / HPF]
- Dysmorphic erythrocytes [number / HPF]
- Epithelial cells [number / HPF]
- Bacteria [number / HPF]
- Yeasts [number / HPF]
- Casts [number / HPF]
- Crystal [number / HPF]

Microscopic Urinalysis is performed if the dipstic results of macroscopic urinalysis show protein, ketones or blood greater than negative or glucose greater than normal.
[Last value ≤ day of randomization will be displayed.]

Table 8 Other Laboratory Variables at Baseline by Treatment Group – SP

totl_t_sp: Other Laboratory Data at Baseline by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract <DATE>

The same layout as in Table 3 will be used. The following variables will be displayed:

- ESR [mm/h (1st hour)]
- CRP [mg/L]
- Anti-dsDNA Antibodies (Negative, Positive)
- HLA-B27 (Negative, Positive)
- HBsAg (Negative, Positive)
- HBsAb* (Negative, Positive)
- HBcAb* (Negative, Positive)
- HBV DNA PCR** (Below detection sensitivity, Meeting/exceeding detection sensitivity)

*If HBsAg is negative, HBsAb and HBcAb Total to be tested.
** Subjects with HBsAg negative, HBsAb negative, and HBcAb Total positive require PCR qualitative testing for HBV DNA
[Last value ≤ day of randomization will be displayed.]

Table 9 Prior Medication by Treatment Group - SP

tpm_t_sp: Prior Medication by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safety Population – Data Extract: <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Prior drug therapies for axSpA	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
n	xxx		xxx		xxx	
All other prior drug therapies	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
xxx	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
n	xxx		xxx		xxx	

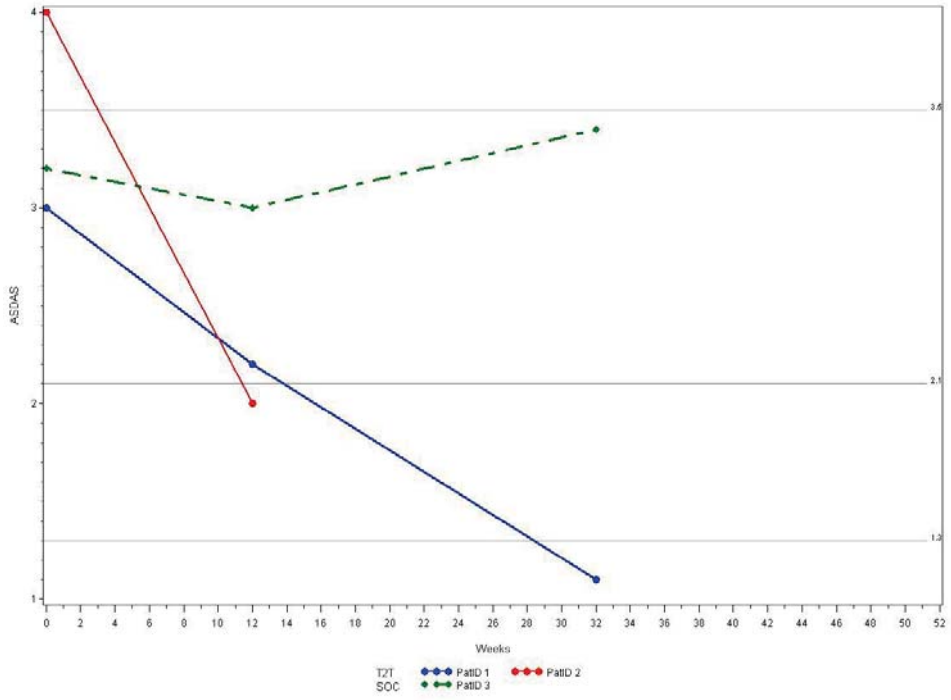
IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

3. TEMPLATES FOR EFFICACY ANALYSES

Figure 1 Ankylosing Spondylitis Disease Activity Score ($ASDAS_{CRP}$) by Treatment Group - SP

fasdascrp_t_sp: Ankylosing Spondylitis Disease Activity Score ($ASDAS_{CRP}$) by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Safetyt Population – Data Extract: <DATE>



IST GmbH Q:\program
<DATE> <TIME> Q:\output

Figure 2 Ankylosing Spondylitis Disease Activity Score ($ASDAS_{ESR}$) by Treatment Group - SP

Same layout as Figure 1

4. TEMPLATES FOR SAFETY DATA

Table 10 Overview of Treatment-emergent Adverse Events by Treatment Group - SP

toae_t_sp: Overview of Treatment-emergent Adverse Events by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Number of patients with at least one AE*	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Malignancy**	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
SAE	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to hospitalization	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to death	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
XXX						
AEs possibly related to HUMIRA	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to withdrawal of HUMIRA	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to interruption of HUMIRA	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to start of co-medication or therapy	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to discontinuation of co-medication or therapy	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
AEs leading to study discontinuation	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)

Percentages are based on N.
* Includes AEs that start either on or after randomisation and any AE ticked as related to study treatment.
**AEs fulfilling criterion for malignancy and patient is <=30 years at time of onset of AE

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Table 11 Treatment-emergent Adverse Events by Treatment Group - SP

tae_t_sp: Treatment-emergent Adverse Events by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

	T2T (N=)	SOC (N=)	Total (N=)
Any AE*	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx

Percentages are based on N.
"xxx (xxx.x), xxx" represents the number of patients with the relevant event, the percentages of patients with the relevant event and the number of the relevant events.
Investigator text for adverse events encoded using MedDRA version xx.x.
* Includes AEs that start either on or after randomisation and any AE ticked as related to study treatment.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Table 12 Treatment-emergent Adverse Events by Severity and Treatment Group - SP

taes_t_sp: Treatment-emergent Adverse Events by Severity and by relationship to study drug - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

<Severity: Mild, Modereate, Severe>

	T2T (N=)	SOC (N=)	Total (N=)
Any AE*	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx

Percentages are based on N.
"xxx (xxx.x), xxx" represents the number of patients with the relevant event, the percentages of patients with the relevant event and the number of the relevant events.
Investigator text for adverse events encoded using MedDRA version xx.x.
* Includes AEs that start either on or after randomisation and any AE ticked as related to study treatment.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Table 13 Treatment-emergent Non-serious Adverse Events by Treatment Group - SP

tnsae_t_sp: Treatment-emergent Non-serious Adverse Events by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

	T2T (N=)	SOC (N=)	Total (N=)
Any AE*	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
System Organ Class 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 1	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
PT 2	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx
xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx	xxx (xxx.x) , xxx

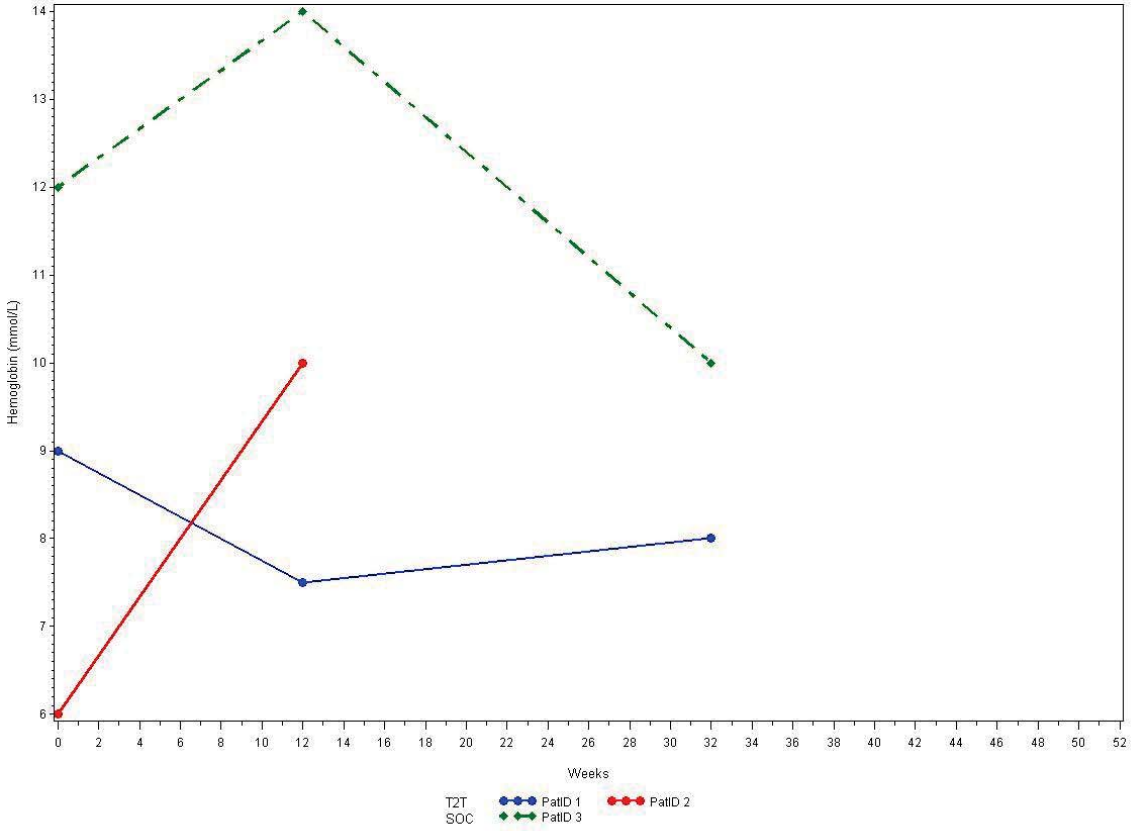
Percentages are based on N. "xxx (xxx.x), xxx" represents the number of patients with the relevant event, the percentages of patients with the relevant event and the number of the relevant events.
Investigator text for adverse events encoded using MedDRA version xx.x.
* Includes AEs that start either on or after randomisation and any AE ticked as related to study treatment. Only preferred terms are taken into account that occurred at a frequency of >=5% in any treatment group.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Figure 3 Laboratory Hematology by Treatment Group – SP

flh_t_sp: Laboratory Hematology by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

Hemoglobine (mmol/L)



The following variables will be displayed:

- Hematocrit [ratio]
- Hemoglobin [g/L]
- Red Blood Cell Count [RBC in [10**12/L]]
- White Blood Cell Count [WBC in [10**9/L]]
- Neutrophils [10**9/L]
- Bands [10**9/L]
- Lymphocytes [10**9/L]
- Monocytes [10**9/L]
- Basophils [10**9/L]
- Eosinophils [10**9/L]
- Platelets [10**9/L]

Figure 4 Laboratory Clinical Chemistry by Treatment Group - SP

```
flc_t_sp: Laboratory Clinical Chemistry by Treatment Group  – SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>
```

Same lay out as in Figure 3 will be used. The following variables will be displayed:

- Creatinine [micromol/L]
- Total Bilirubin [micromol/L]
- Total Bilirubin / ULN
- Albumin [g/L]
- AST [U/L]
- AST / ULN
- ALT [U/L]
- ALT / ULN
- Glucose [mmol/L]

Figure 5 Laboratory Microscopic Urinalysis by Treatment Group – SP

flmu_t_sp: Laboratory Microscopic Urinalysis by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

Same lay out as in Figure 3 will be used. The following variables will be displayed:

- Leucocytes [number / HPF]
- Erythrocytes [number / HPF]
- Dysmorphic erythrocytes [number / HPF]
- Epithelial cells [number / HPF]
- Bacteria [number / HPF]
- Yeasts [number / HPF]
- Casts [number / HPF]
- Crystal [number / HPF]

Figure 6 Vital Signs by Treatment Group - SP

fvs_t_sp: Vital Signs by Treatment Group – SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

The same layout as in Figure 3 will be used. The following variables will be displayed:

- Systolic blood pressure [mmHg]
- Diastolic blood pressure [mmHg]
- Pulse [bpm]
- Respiratory rate [breath per minute]
- Body temperature [°C]
- Weight [kg]
- BMI [kg/sqm]

Table 14 Laboratory Macroscopic Urinalysis by Treatment Group – SP

tlmu_t_sp: Laboratory Macroscopic Urinalysis by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

<Parameter>

Tretment Group	Week	n	Classification									
			Level 1		Level 2		Level 3		Level 4		Level xxx	
T2T (N=)	Day 1	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	Week 2	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	Week 4	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	XXX	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
SOC (N=)	Day 1	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	Week 2	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	XXX	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Total (N=)	Day 1	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	Week 2	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
	XXX	xxx	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)

Percentages are based on n (number of valid values)

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

The following variables will be displayed:

- Specific Gravity (1.005, 1.010, 1.015, 1.020, 1.025, 1.030, NA/ND)
- Ketones (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Protein (Negative, Trace, +, ++, +++, ++++, NA/ND)
- Glucose (Negative, Trace, +, ++, +++, ++++, NA/ND)
- pH (4.5, 5, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, NA/ND)
- Nitrite (Negative, Positive, NA/ND)
- Blood (Negative, Trace, +, ++, +++, ++++, NA/ND)

Figure 7 Other Laboratory Tests by Treatment Group - SP

```
flo_t_sp: Other Laboratory Tests by Treatment Group  - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>
```

The same layout as in Figure 3 will be used. The following variables will be displayed:

- ESR [mm/h (1st hour)]
- CRP [mg/L]

Table 15 Concomitant Medication by Treatment Group - SP

tcmd_t_sp: Concomitant Medication by Treatment Group - SP
Protocol(s): W15-679 - STRIKE
Analysis: Saftey Population – Data Extract: <DATE>

	T2T (N=)		SOC (N=)		Total (N=)	
Concomitant Medication						
Number of patients with any Concomitant Medication taken	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 1	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 2	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 3	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 4	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 5	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 6	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
Drug Name 7	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)
XXX	xxx	(xxx.x)	xxx	(xxx.x)	xxx	(xxx.x)

Percentages are based on N. Concomitant medications are defined as all medication **except** medication for axSpA.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

5. TEMPLATES FOR GLOSSARIES

Table 16 Glossary of System Organ Class, MedDRA Preferred Terms and Verbatim Terms for Adverse Events or Diseases

tgae: Glossary of System Organ Class, MedDRA Preferred Terms and Verbatim Terms for Adverse Events or Diseases
Protocol(s): W15-679 - STRIKE
Analysis: Data Extract: <DATE>

System Organ Class	Preferred Term	Lower Level Term	Verbatim Term
xxx	xxx		xxx
	xxx		xxx
			xxx
xxx			

MedDRA Version x.x

Table 17 Glossary of Preferred Terms and Verbatim Terms for Concomitent Medication

tgcom: Glossary of Preferred Terms and Verbatim Terms for Concomitent Medication
Protocol(s): W15-679 - STRIKE
Analysis: Data Extract: <DATE>

Preferred Term	Dictonary Drug Name	Verbatim Term
xxx	xxx	xxx
	xxx	xxx
		xxx
xxx		

MedDRA Version x.x

6. TEMPLATES FOR LISTINGS

Listing 1 Patient Disposition

ldis_en: Patient Disposition
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

Patient No	Date informed consent signed	All inclusion/ No exclusion criteria met	Re-screened [previous number]	Randomization date	Reason why not randomized	Treatment group	Received treatment for axSpA after randomization	Completed the treatment phase [reason why not]	Major Protocol violations
xxx	xxx	Yes	xxx	xxx	xxx	xxx	xxx	No - xxx*	
xxx	xxx	No							
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	

*primary reason

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

Listing 2 Inclusion and Exclusion Criteria

lie_en: Inclusion and Exclusion Criteria
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

Patient No	Treatment Group	Inclusion Criteria Not Met/ Exclusion Criteria Met
xxx	xxx	xxx
xxx	xxx	xxx
xxx	xxx	xxx
xxx	xxx	xxx
xxx	xxx	xxx
xxx	xxx	xxx
xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

Listing 3 Baseline Demographic Characteristics

ldm_en: Baseline Demographic Characteristics
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group> Patient No	Sex	Year of birth	Age	Height [cm]	Weight [kg]	BMI [kg/sqm]
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	

Listing 4 Medical and Surgical History: Tobacco or Alcohol Use

ltau_en: Medical and Surgical History: Tobacco or Alcohol Use
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group> Patient No	Tobacco/ Alcohol use		Number of years	Number of packs per day/ Frequency of drinks*	Year stopped
xxx	Cigarettes	current	xxx	xxx	xxx
	Pipes	never			
	Cigars	never			
	Alcohol	never			
xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx

* One drink is defined as 10 ml (or approximately 8 grams) of pure alcohol and equals: 200 ml of beer or 100 ml of wine or 20 ml of hard liquor

Listing 5 Medical and Surgical History: Axial Spondyloarthritis and Other History

lhao_en: Medical and Surgical History: Axial Spondyloarthritis and Other History
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group>

Patient No	Date of SpA Sympt. started	Date of axSpA diagnosis				
	Medical History for axSpA U/I/P/OM	Other medical History (OM)	Surgical History for axSpA Sp/Jr/Js/A/OS	Other surgical History (OS)	Other features of spondyloarthritis	
xxx	xx/xx/xxxx	xx/xx/xxxx				
	Never/Unknown/Former/ No		No/No/No/Yes	xxxxxxxxxxx	Inflammatory back pain	Yes
					Age at onset < 40 Yrs	Yes
					Insidious onset	Yes
					Improvement with exercise	Yes
					No improvement with rest	Yes
					Night pain with improve. upon getting up	Yes
					Arthritis (past)	No
					Heel enthesitis (past)	Yes
					Good prior resp. to NSAIDS*	No
					Family history of SpA	-
xxx	xx/xx/xxxx	xx/xx/xxxx				
	xxxx/xxxx/xxxx/Yes	xxxxxxxxx	xxx/xxx/xxx/No		Inflammatory back pain	No
					Age at onset < 40 Yrs	No
					…	
…						

* (back pain is not present anymore or much better 24 to 48 hours after a full dose of an NSAID)
U – uveitis, I – inflammatory bowel disease (CD, UC only), P - psoriasis, OM - other medical history
Sp – spinal surgery, Jr – joint replacement, Js – joint surgery, A – arthroscopy, OS – other surgical history

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 6 Prior Medication for axSpA

lpma_en: Prior Medication for axSpA
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group>

Patient No	Medication name	Day of first dose	Date of first dose	Date of last dose	Ongoing at start of study	Maximum dose taken	Unit	Frequency	Route of administration	Reason for discontinuation
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 7 All Other Prior Medication

lopm_en: All Other Prior Medication
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group>

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at start of study	Dose	Unit	Frequency	Route of administration	Reason for use
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 8 Treatment Exposure

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

T2T: NSAID

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Dose	Unit	Frequency	Route of administration	Reason for use
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

NSAIDs administered for treatment of axSpA following the T2T intensified schedule.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

T2T: Adalimumab

Patient No	Week study drug administered	Date and time	Day	Injection site	Was entire volume injected?	Reason dose skipped	Decision to start adalimumab	Delay*
xxx	First Injection	xxx	xxx	xxx	xxx	xxx	xxx	xxx
	2 weeks after 1st injection XXX	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

* number of days between decision to start adalimumab and first injection

IST GmbH Q:\program
<DATE> <TIME> Q:\output

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

SOC: Non-Selective NSARs

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Dose	Unit	Frequency	Route of administration
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx

All medications for treatment of axSpA that were started after start of study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

SOC: COX-2 Inhibitors

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Dose	Unit	Frequency	Route of administration
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx

All medications for treatment of axSpA that were started after start of study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

SOC: DMARDs

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Average dose	Unit	Frequency	Route of administration
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx

All medications for treatment of axSpA that were started after start of study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

SOC: Biologicals

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Dose	Unit	Frequency	Route of administration
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx

All medications for treatment of axSpA that were started after start of study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

lte_en: Treatment Exposure
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

SOC: Other

Patient No	Medication name	Day of start	Start date	Stop date	Ongoing at end of study	Dose	Unit	Frequency	Route of administration
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx

All medications for treatment of axSpA that were started after start of study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

Listing 9 Concomitant Medication

The same layout as in Listing 7 will be used:

All medications, except medications for treatment of axSpA, that were started after start of study.

Listing 10 Adverse Events

lae_en: Adverse Events
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment Group>

Patient No	Day of onset	Onset date	AE preferred term	End date of event/ Ongoing at the end of study	Severity of the event	Is the AE IN/S/M/PC/R/OC?	Seriousness criteria L/D/H/I/P/C	Date of death	Actions taken HW/HI/CS/CD/DS/OA	Specification for Other cause of event (OC)/ Other actions taken (OA)/ Cause of Death (D)
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					
xxx	xxx	xxx	xxx	xxx	xxx					

IN-Intermittent, S-Serious, M-Malignant, PC-Associated with a product complaint, R-Possibily related to HUMIRA, OC-Caused by something else, L- Life-threatening, D-Death, H-Hospitalization or prolongation of hospitalization, I-Important medical event requiring medical or surgical intervention to prevent serious outcome (includes spontaneous and elective abortion), P-Persistent or significant disability/incapacity, C-Congenital anomaly, HW-HUMIRA withdrawn permanently, HI-HUMIRA interrupted,
CS-Concomitant medication or therapy started, CD-Concomitant medication or therapy discontinued, DS-Discontinued study, OA-Other action taken

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

For the following listings the same layout as in Listing 10 will be used:

Listing 11 Malignancy

*AEs fulfilling criterion for malignancy and patient is <=30 years at time of onset of AE

Listing 12 Serious Adverse Events

*including AEs where specifications regarding seriousness are missing

Listing 13 Adverse Events Leading to Death

Listing 14 Adverse Events Leading to Hospitalization

Listing 15 Adverse Events Possibly Related to HUMIRA

Listing 16 Adverse Events Leading to Permanent Withdrawal from HUMIRA

Listing 17 Adverse Events Leading to Interruption of HUMIRA Intake

Listing 18 Pregnancy Test

lpt_en: Pregnancy Test
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

Patient No	Pregnancy test performed	Reason why not	Day pregnancy test performed	Date pregnancy test performed	Result of urine pregnancy test	Result of serum pregnancy test
xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx

If result of urine pregnancy test is positive, a serum pregnancy test is to be performed. If result of serum pregnancy test is positive, the patient is not eligible for continuation in this study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

Listing 19 Laboratory Clinical Chemistry

llc_en: Laboratory Clinical Chemistry
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

Patient No	Time Window	Day of sample collection	Sample collection date	Parameter	Result	Unit	Upper limit of normal	SI result	SI Unit
xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx		xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 20 Laboratory Hematology

The same layout as in Listing 19 will be used:

Listing 21 Macroscopic Urinalysis

lmau_en: Macroscopic Urinalysis
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day of sample collection	Sample collection date	Parameter	Dipstick result	Microscopic Urinalysis Required per protocol	Reason why required per protocol but NOT performed
xxx		xxx	xxx	xxx	xxx	xxx	xxx
xxx		xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 22 Microscopic Urinalysis

lmiu_en: Microscopic Urinalysis
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day of sample collection	Sample collection date	Parameter	Result [number/HPF]
xxx		xxx	xxx	xxx	xxx
xxx		xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 23 ESR/CRP

The same layout as in Listing 19 will be used:

Listing 24 Hepatitis B Testing

The same layout as in Listing 22 will be used:

Listing 25 Vital Signs/ Weight

lvs_en: Vital Signs/ Weight
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day of sample collection	Sample collection date	Systolic / Diastolic blood pressure [mmHg]	Pulse [bpm]	Respiratory rate [breaths per minute]	Body temperature [°C]	Weight [kg]	BMI [sqm]
xxx	xxx	xxx	xxx	xxx/xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx/xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

Listing 26 Dactylitis

lda_en: Dactylitis
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day of sample collection	Sample collection date	Dactylitis	Dactylitis count	Digits hands	Right hand	Left hand	Digits feet	Right foot	Left foot
xxx	xxx	xxx	xxx	Yes	15	Thumb	Absent	Present	Great toe	Absent	Present
						Index	xx	xx	Second	xx	xx
						xxx					
xxx	xxx	xxx	xxx	No							

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 27 Anterior Uveitis

lau_en: Anterior Uveitis
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day of initial diagnosis/ new onset	Date of initial diagnosis/ new onset	Anterior uveitis confirmed by an ophthalmologist/ New onset	Number of flares within the prior 12 months/ since last visit	Eye(s)	Date of the most recent flare*	Treatments received in the past for anterior uveitis*
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	

* Reported during screening only.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 28 Physical Examinations

The same layout as in Listing 26 will be used:

Listing 29 ECG

The same layout as in Listing 26 will be used:

Listing 30 Tuberculosis

ltb_en: Tuberculosis
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

Patient No	Infected with TB in the past	Higher risk for TB	Former BCG vaccination	IGRA test performed before initiating T2T escalation step 2	Day and Date of blood drawn for TB blood test	Result	Type of test	TB prophylaxis required	Enrolled on TB prophylaxis
xxx	xxx	xxx	xxx	xxx		xxx	xxx	xxx	Yes - Isoniazid 5 mg/kg
xxx	xxx	xxx	xxx	xxx		xxx	xxx	xxx	No

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 31 Chest X-Ray

lxr_en: Chest X-Ray
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

T2T Patient No	Chest X-ray performed before initiating T2T escalation step 2	Reason why not	Day and Date of chest X-ray	Performed by a radiologist	Parameter	Result	Specification of other clinically significant findings
xxx	xxx		xxx	xxx	Calcified granuloma	Present	xxx
					Pleural scarring	xxx	
					Pleural thickening	xxx	
					Signs of active TB	xxx	
					Signs indicative of previous TB infection	xxx	
					Other clinically significant findings	xxx	
xxx	xxx				xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output

Listing 32 Ankylosing Spondylitis Disease Activity Score (ASDAS)

lasd_en: Ankylosing Spondylitis Disease Activity Score (ASDAS)
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

Patient No	Time Window	ASDAS (CRP)	ASDAS (ESR)	Total back pain (BASDAI question 2)	Patient global assessment of disease activity	Peripheral pain/swelling (BASDAI question 3)	Duration of morning stiffness (BASDAI question 6)	Erythrocyte sedimentation rate [mm/hr]	C-reactive Protein (mg/L)
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output

PAGE X OF X

Listing 33 Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

lbas_en: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

Patient No	Time Window	Day	Date	BASDAI	Answers Q1 | Q2 | Q3 | Q4 | Q5 | Q6
xxx	xxx	xxx	xxx	xxx	X | X | X | X | X | X
xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	
xxx	xxx	xxx	xxx	xxx	

Q1 - How would you describe the overall level of fatigue/tiredness you have experienced?
Q2 - How would you describe the overall level of AS NECK, BACK OR HIP pain you have had? (0=none to 10=very severe)
Q3 - How would you describe the overall level of pain/swelling in joints OTHER THAN neck, back, or hips you have had? (0=none to 10=very severe)
Q4 - How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure? (0=none to 10=very severe)
Q5 - How would you describe the overall level of morning stiffness you have had from the time you wake up? (0=none to 10=very severe)
Q6 - How long does your morning stiffness last from the time you wake up? (0=0hrs .. 5=1hrs .. 10=>=2 hrs)

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 34 Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)

lmas_en: Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day	Date	MASES	Patient Right 1CL|7CL|PSIS|ASIS|IC|PIAT|5LSP	Patient Left 1CL|7CL|PSIS|ASIS|IC|PIAT|5LSP
xxx	xxx	xxx	xxx	xxx	A | P | N | X | X| X | X	A | P | N | X | X| X | X
xxx	xxx	xxx	xxx	xxx		
xxx	xxx	xxx	xxx	xxx		
xxx	xxx	xxx	xxx	xxx		

A - Absent, P – Present, N – No assessment
1CL – 1st Costochondral joint, 7CL - 7th Costochondral joint, PSIS - Posterior superior iliac spine, ASIS - Anterior superior iliac spine, IC -Iliac crest, PIAT - Proximal insertion of achilles tendon, 5LSP - 5th Lumbar spinous process

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 35 ASAS Health Index (HI)

The same layout as in Listing 33 will be used:

Listing 36 ASAS20, ASAS40 and ASAS Partial remission

The same layout as in Listing 32 will be used:

Listing 37 Bath Ankylosing Spondylitis Functional Index (BASFI)

The same layout as in Listing 33 will be used:

Listing 38 Bath Ankylosing Spondylitis Metrology Index (BASMI lin)

The same layout as in Listing 34 will be used:

Listing 39 EQ-5D

The same layout as in Listing 33 will be used:

Listing 40 WPAI-axSpA

The same layout as in Listing 33 will be used:

Listing 41 Physician's/Patient's Assessment, NRS

lpa_en: Physician's/Patient's Assessment, NRS
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day	Date	Assessment	Result
xxx	xxx			Physician's Global Assessment of Disease Activity	
				Patient's Global Assessment of Disease Activity	
				Patient's Assessment of Nocturnal Back Pain	
				Patient's Assessment of Total Back Pain	
				Patient's Global Assessment of Pain	
xxx	xxx				
xxx	xxx				
xxx	xxx				

0= noe to 10 = severe

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 42 Baseline MRI with Investigator Assessments

lmribl_en: Baseline MRI with Investigator assessments
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group>

	MRI of spine				MRI of SI joints				
Patient No	Day/ Date	Signs of Active Infl.	Signs of Chronic Infl.	Reason why, if MRI not performed	Day/ Date	Signs of Active Infl.	Signs of Chronic Infl.	Reason why, if MRI not performed	Structural changes visible
xxxx	xx/ xxxxx	Yes	No		xx/ xxxxx	Yes	No		Erosion Fat metaplasia Bone marrow edem/osteitis
xxxx	xx/ xxxxx	Yes	Yes		xx/ xxxxx	Yes	No		Sclerosis Erosion Fat metaplasia Bone marrow edem/osteitis
xxxxxx	xx/ xxxxx	xxx	xxx		xx/ xxxxx	xx	xx		xxxxxxx

IST GmbH Q:\program
<DATE> <TIME> Q:\output

Listing 43 Berlin MRI Score for MRI of Sacroiliac Joint

lmsj_en: Berlin MRI Score for MRI of Sacroiliac Joint
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

Patient No	Time Window	Day	Date		Score	Quadrant I L | R	Quadrant II L | R	Quadrant III L | R	Quadrant IV L | R	Total L | R
xxx	xxx	xxx	xxx	Active inflammation	xx	xx |xx	xx |xx	xx |xx	xx |xx	
				Erosion	xx	xx | xx	xx |xx	xx |xx	xx |xx	
				Fatty disposition	xx	xx | xx	xx |xx	xx |xx	xx |xx	
				Sclerosis	xx					xx |xx
				Ankylosis	xx					xx |xx
xxx	xxx									
xxx	xxx									
xxx	xxx									

MRI of the sacroiliac (SI) joints was evaluated at screening and the last visit (at week 52 visit or – in case of early discontinuation – the discontinuation visit). Not all patients had an MRI for the last visit due to the early stop of the study.

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X

Listing 44 Berlin MRI Score for MRI of Spine

The same layout as Listing 43 will be used:

Listing 45 Tender and Swollen Joints

lts_en: Tender and Swollen Joints
Protocol(s): W15-679 - STRIKE
Analysis: Enrolled Population - Data Extract: <DATE>

<Treatment group> Patient No	Time Window	Day	Date	Tender joint counts	Swollen joint counts	Joint	Right PT | S | J	Right PT | S | J
xxx	xxx	xxx	xxx	xx	xx	Temporomandibular	A | P | N	A | P | R
						Sternoclavicular		
						Acromio-clavicular		
						XXX		
xxx	xxx							
xxx	xxx							
xxx	xxx							

A - Absent, P - Present, R - Replaced, N - No Assessment, PT - Pain/Tenderness, S - Swelling, J - Joint

IST GmbH Q:\program
<DATE> <TIME> Q:\output PAGE X OF X