Protocol B1801023

AN OPEN-LABEL EXTENSION STUDY TO ASSESS THE LONG-TERM SAFETY AND CLINICAL BENEFIT OF ETANERCEPT IN CHILDREN AND ADOLESCENTS WITH EXTENDED OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS, ENTHESITIS-RELATED ARTHRITIS, OR PSORIATIC ARTHRITIS WHO WERE PREVIOUSLY ENROLLED IN PROTOCOL 0881A1-3338-WW (B1801014)

Statistical Analysis Plan (SAP)

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Revision History

Version	Date	Author(s)	Summary of Changes/Comments
1	2Dec2011	PPD PPD	First version based on original protocol (25 Feb 2011)
2	08Apr2013	PPD	Based on Protocol Amendment 1 (20 Jul 2012), the following changes were made: Title: • Added "AND CLINICAL BENEFIT" Section 2.1: • Added an additional secondary objective. [redacted] • Added the withdrawal/Re-treatment period Section 3: • FAAS, OAAS, and OOAS were removed. Section 3.2: • Added Withdrawal Analysis Set Section 3.3: • Added Re-treatment Analysis Set Section 4.2.2: • Added additional endpoints for subjects in the active treatment period, withdrawal/re-treatment period. Section 5.2: • Treatment-emergent event definition was added. Section 5.4: • Added additional baseline disease characteristics. Section 5.8: Added analysis method for categorical endpoints. Section 5.16 was added.

3	14-Apr-2015	PPD	Section 4.0.1 added to address site specific data exclusion for 1 subject to address lost source documents
4.0	8-Mar-2017	PPD	CCI [redacted]

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1. INTRODUCTION

[Note: In this document, any text taken directly from the protocol is italicized.]

The purpose of this document is to provide further details about the statistical analysis methods specified in the study protocol B1801023. *Protocol B1801023 is an 8-year extension study designed to further characterize the long-term safety profile, malignancy and other serious adverse events, and clinical benefit for those pediatric subjects who received at least one dose of etanercept and completed 96 weeks of investigational product and/or follow-up in study 0881A1-3338-WW (B1801014). The previous study was designed to assess the clinical benefit and the long-term safety of etanercept for 2 years* (96 weeks) *in pediatric subjects with extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).*

Based on the lack of information regarding when treatment with etanercept should be discontinued and the success of re-treatment if relapse occurs, this protocol is being amended to also explore clinical benefit and physical function after withdrawal of etanercept and after disease relapse occurs.

A brief description of the study objectives and the study design are given in Section 2. Subsequent sections include the definitions of baseline, efficacy and safety endpoints, and analysis populations followed by details about statistical methods. Any major deviations from the methods specified in this document and the protocol must be discussed in the clinical study report.

In order to evaluate overall safety in the most meaningful way, data from the 8 year extension study should not be analyzed independent of the data collected during the preceding 2 year parent study. Therefore, most of the safety analyses will be based on the combined data from the parent study and the subsequent extension. The resulting data summaries and analyses will cover the entire period of up to 10 years. In some cases, in order to fully address the entire etanercept experience, data from subjects who were in the parent study but were never enrolled in the extension study will be included in determining overall rates. Details will be provided in the following sections.

2. STUDY OBJECTIVES AND STUDY DESIGN

2.1. Objectives

Primary

To monitor the occurrence of malignancy in pediatric subjects with eoJIA, ERA, or PsA.

Secondary

- *To assess the long-term safety profile of etanercept;*
- *To evaluate the long-term effect of etanercept on clinical benefit and physical function.*

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2.2. Study Design

2.2.1. Basic Features of the Study Design

This is an open-label, single treatment, multi-center, 8-year extension study in pediatric subjects who have been diagnosed with one of 3 subtypes of JIA (eoJIA, ERA, or PsA), have received at least one dose of etanercept and completed approximately 96 weeks of participation in study 0881A1-3338-WW (B1801014). These subjects will be asked to participate in study B1801023. It is anticipated that approximately 100 subjects will be enrolled in study B1801023. This 96-month study contains 3 periods: an active treatment period, a withdrawal/re-treatment period, and an observational period.

Active treatment period

Subjects who completed approximately 96 weeks of active treatment with investigational product (etanercept) in study 0881A1-3338-WW (B1801014) and are eligible to continue investigational product in study B1801023 will enter directly into the active treatment period. These subjects may continue to receive investigational product for up to 8 additional years (96 months).

Withdrawal/Re-treatment period

Withdrawal: Subjects who have either completed approximately 96 weeks of treatment in study 0881A-3338 or were enrolled in the active treatment period of study B1801023 and who have either met the Wallace definition for clinically inactive disease for at least 6 months on investigational product (etanercept) or who, in the investigators judgment, have had a good clinical response and would benefit from withdrawal from investigational product and are otherwise eligible can enter the withdrawal/re-treatment period. However, the withdrawal/re-treatment period is optional and it is ultimately up to the investigator and subject to determine when the subject should be withdrawn from treatment.

Re-treatment: Subjects requiring re-treatment per the investigator's clinical judgment and who are otherwise eligible will be offered the option to re-start treatment with investigational product.

Subjects may not enter the withdrawal/re-treatment period more than once during the study.

Observational period

All subjects will be followed for a total of 8 years from the time of initial entry into the study as follows:

Subjects who discontinue investigational product prior to completing 96 weeks of active treatment in study 0881A1-3338-WW (B1801014) for any reason or who are not eligible to continue investigational product in study B1801023 will not be permitted to re-start investigational product in study B1801023 and will be asked to enter the observational period. Subjects who participate in the active treatment period of study B1801023 and subsequently discontinue use of investigational product at any time before completion of the study and do not participate in the withdrawal/re-treatment period for any reason (i.e., ineligible or subject declined participation) will be asked to participate in the observational period. Subjects who participate in the withdrawal period and are ineligible for re-treatment with investigational product for any reason will be asked to participate in the observational period. Subjects who participate in the re-treatment period and subsequently discontinue investigational product prior to the completion of the study will be asked to participate in the observational period.

Once a subject enters into the observational period, he or she cannot resume investigational product for the remaining time in the study. Subjects participating in the observational period of study B1801023 may receive standard of care including any anti-TNF agents (eg, commercial etanercept) and/or other biologic agents for treatment of their disease at the discretion of the investigator.

2.2.2. Interim Analysis

No formal statistical interim analyses are planned. However, a descriptive analysis will be performed at a minimum of every 2 years based on the time of last patient first visit. In addition, summaries of safety and efficacy assessments will be produced at intervals to satisfy regulatory obligations and the requirements of the Internal Review Committee.

2.2.3. Sample Size Rationale

The sample size for this safety extension protocol, as agreed upon with regulatory authorities, is not based on efficacy considerations; rather, all eligible subjects who either complete or discontinue from study 0881A1-3338-WW (B1801014) will be asked to participate in study B1801023. The anticipated enrollment is approximately 100 subjects.

3. ANALYSIS SETS

3.1. Full Analysis Set

The full analysis set (FAS) will include all subjects in the parent study who received at least one dose of investigational product regardless of whether they received any investigational product during the extension study.

3.1.1. Site specific exclusion from full analysis set.

Source data for three Study visits M6, M9 and M12 of Pt 10081010 in Hungary, were accidentally lost at site. Duplicate patient charts could be reconstituted from the computerized data base of the hospital, but outcome data and patient dosing diary data for the three patient visits were lost and could not be recovered. The team decided that data deletion from the system is not recommended. However, the decision was made that all patient safety data will be included in the study report but not the efficacy data for the three visits.

3.2. Withdrawal Analysis Set

The withdrawal analysis set (WAS) will include those subjects who entered the withdrawal period. Only data collected in the withdrawal period will be included.

3.3. Re-treatment Analysis Set

The re-treatment analysis set (RTAS) will include those subjects who entered the re-treatment period. Only data collected in the re-treatment period will be included.

4. SPECIFICATION OF ENDPOINTS AND VARIABLES

The primary endpoints in this study are related to safety. Efficacy endpoints are secondary.

4.1. Demography and Baseline Characteristics

The demographic data include age, sex, race, weight, height and BMI. The baseline characteristics are: subtype of JIA, disease duration, number of prior DMARDS, use of the following medications: DMARDS, methotrexate, HCQ, chloroquine, SSZ, oral corticosteroids and oral NSAIDS.

4.2. Endpoints

4.2.1. Primary

The occurrence of malignancy is the primary endpoint for all subjects.

4.2.2. Secondary Endpoints

The secondary endpoints include

- *the occurrence of serious adverse events* (SAE, infectious and non-infectious events will be summarized separately),
- *the occurrence of medically important infections (ie, an infection requiring hospitalization and /or parenteral [intravenous (IV), intra-muscular (IM)] anti-infective agents).*
- Hospitalization: For any hospitalizations, the admission date, discharge date and reason for hospitalization will be collected during the study.
- Death: For any deaths, date of death and cause of death will be collected during the study.

- Nonstudy medication: nonstudy medications are coded using the WHO Drug Dictionary (2006 Q3). The Prior, Concomitant, After (PCA) flag for nonstudy medications will be derived for both parent study and extension study (only for active treatment period):

    - Prior nonstudy medications are defined as any nonstudy medications taken before the first dose of investigational product taken at the start of the study,

    - Concomitant nonstudy medications are defined as any nonstudy medications taken during the treatment period (from the first dose to the last dose of the investigational product).

    - After nonstudy medications refer to any nonstudy medications taken after the last dose of the investigational product.(not applicable for observational period)

- Exposure: the total number of doses taken and exposure time.

The above endpoints will be collected for all subjects. The following endpoints will be collected only for subjects in the active treatment period, or withdrawal/re-treatment period in the extension study:

Non-serious adverse Events (Adverse events that occur up to 30 days after the last dose of investigational product will be counted as having occurred during the treatment period) This is applied for active and retreatment periods. If an AE started in active or retreatment period and continued into withdrawal or observational period, it will be only counted in active or retreatment period, it will not be counted in withdrawal or observational period again. If an event started in withdrawal or observational period, and after 30 days of the last dose of investigational product of active period or re-treatment period, this event will not be counted.
Occurrence of withdrawals from investigational product due to adverse events;
Laboratory evaluations (ie, hematology, blood chemistry, and CRP)
Tanner Stage Assessment for subjects <18 years of age or who have a score of <5 on 1 or more applicable domain(s). The Tanner Assessment does not need to be repeated if it was performed within 2 months before the early withdrawal visit.
Vital Signs: Temperature, blood pressure (mmHg) and pulse rate (beats/min, after sitting for at least 5 minutes);
Growth parameters: height, weight, BMI;

- Efficacy:

    - *ACR Pediatric 30, 50, 70, 90, and 100, defined as ≥ 30% (and 50%, 70%, 90%,100%, respectively) improvement from baseline in at least 3 of the 6 following variables, with no more than 1 of the remaining variables worsening by > 30 %:*

        - *Physician's Global Assessment (PGA) of Disease Activity on a 21-circle visual analogue scale (VAS);*

        - *Patient/Parent Global Assessment on a 21-circle VAS;*

        - *Childhood Health Assessment Questionnaire (CHAQ*

- *Number of joints with active arthritis, defined as joints that are swollen or, in the absence of swelling, joints with limited range of motion accompanied by pain and/or tenderness;*
- *Number of joints with limited range of motion;*
- *Laboratory measure of inflammation, c-reactive protein (CRP);*

(Note: ACRPedi responses will be calculated based on parent study baseline. For subjects aged ≥18 years, CHAQ is missing)

- *Individual components of the ACR Pediatric Assessments;*
- *Pain Assessment on a 21-circle VAS;*
- *Duration of morning stiffness in minutes;*
- *Clinically inactive disease defined as follows per 2011 Wallace Criteria:*
    - *No joints with active arthritis (defined as joints that are swollen or, in the absence of swelling, joints with limited range of motion accompanied by pain and/or tenderness);*
    - *No fever, rash, serositis, splenomegaly, or generalized lymphadenopathy attributable to JIA;*
    - *No active uveitis;*
    - *CRP level within normal limits in the laboratory where tested or, if elevated, not attributable to JIA;*
    - *PGA of disease activity score of best possible on the scale used;*
    - *Duration of morning stiffness of ≤ 15 minutes;*
- *The Juvenile Arthritis Disease Activity Score (JADAS), using 4 components (PGA of Disease Activity, Patient/Parent Global Assessment, number of joints with active arthritis and CRP).*

- *Additional Secondary Endpoints for ERA Subjects*
  - *Overall Back Pain and Nocturnal Back Pain on a 100 mm VAS;*
  - *Bath Ankylosing Spondylitis Metrology Index (BASMI) components (Intermalleolar Distance, Cervical Rotation, Modified Schober's Test, Lateral Flexion, and Tragus to Wall Distance. Note: Modified Schober's Test is used for BASMI calculation. Schober's Test, not Modified Schober's Test, was collected for this study. So BASMI cannot be calculated for this study).*
- *Additional Secondary Endpoints for PsA Subjects*
  - *Body Surface Area (BSA);*
  - *PGA of Psoriasis.*

- *Health outcomes assessments for Subjects in the Active Treatment Period, and Withdrawal/Re-treatment Period:*
  - *Childhood Health Assessment Questionnaire (CHAQ): for subjects aged <18 years at the time of assessment;*
  - *Health Assessment Questionnaire (HAQ): for subjects aged ≥18 years at the time of assessment.*
  - *Proportion of subjects with total CHAQ score improvement of >0.188 (decrease by >0.188) from baseline of 1014.*

[redacted]

5. ANALYSIS METHODS

All analyses will be performed for the overall population as well as each of the 3 JIA subtypes.

5.1. Data Analysis Intervals

As shown in the study flowchart of the protocol, the visit time and the collection time of study endpoints are regularly scheduled. However, these scheduled time points may not be followed exactly. For the purpose of reporting clinical data results and satisfying the requirements of certain statistical analysis methods, it is necessary to window the actual observation time into data analysis intervals (DAIs). Details regarding the DAIs will be provided in a separate programming specifications document.

5.2. Treatment-emergent Events

An event is defined as a treatment-emergent event if the event occurred during the active period (either parent or extension studies) or re-treatment period with onset dates between the first dose date of investigational product and within 30 days after the last dose of investigational product. If a treatment-emergent event started in active or re-treatment period and continued to withdrawal or observational period, it will be only counted in active or re-treatment period, it will not be counted in withdrawal or observational period again. If an event started in the withdrawal or observational periods, and after 30 days of the last dose of investigational product of the active period or re-treatment period, this event is not a treatment-emergent event.

5.3. Subject Disposition

The numbers (and percentages) of subjects who were enrolled, who took at least one dose of investigational product, who discontinued from the parent study and who completed the parent study will be summarized from FAS. The number who completed the parent study will be further broken down into the number who did and did not continue into the extension study. The numbers (and percentages) of subjects who discontinued from the extension and who completed the extension will be summarized. This will be done separately for all subjects in the extension, for all subjects who began the extension in the active treatment period, withdrawal/re-treatment period, and for subjects who began the extension in the observational period. For those subjects who began in the active treatment period, the numbers who entered withdrawal/re-treatment period, who switched to the observational period, and reason for switching, will also be tabulated. In addition, the proportion of subjects who discontinued from the extension study for any reason and for each specific reason will be tabulated. The number and percentage of subjects who completed each year of the study may be provided.

5.4. Demography and Baseline Characteristics

Demographic, baseline characteristics (eg, subtype of JIA) and baseline disease characteristics (physician global assessment, patient/parent global assessment, Number of joints with LOM, Number of painful joints, Number of swollen joints, Pain assessment, Morning stiffness, CRP, CHAQ and HAQ. Additionally, Tender entheseal score, Overall back pain VAS, Nocturnal back pain VAS, Modified Schober's test for ERA subtype; BSA of psoriasis, Physician's Global Assessment of Psoriasis for PsA subtype) data will be summarized. For continuous variables such as age, height, weight, the descriptive statistics will include the number of patients, mean, median, standard deviation, minimum, and maximum. For dichotomous variables such as sex and nominal variables such as race and ethnicity, the descriptive statistics will include the total number of patients, the count and percentage in each category. Baseline and demographic data will be summarized for subjects entered extension study (both parent study and extension study baselines), Withdrawal Analysis Set

(WAS, withdrawal period baseline), and Re-treatment Analysis Set (RTAS, retreatment period baseline).

5.5. Malignancies, SAE and Medically Important Infections

The malignancies, serious adverse events and medically important infections will be summarized using the frequency and percentage of subjects reporting events. The adjusted rate per 100 subject-years of exposure to etanercept (defined as # of events/total exposure*100) will be summarized also.

The incidence of malignancies may be compared to external data sources to generate standardized incidence ratios (SIRs) to aid interpretation.

In addition to showing cumulative rates over the entire study period (including both parent study and extension), incidences of subjects with malignancies, serious adverse events and medically important infections as well as exposure-adjusted rates will also be categorized by year for each year from 1 through 10.

These summaries and analyses will be performed for:

- FAS, all events in all periods;
- FAS, treatment-emergent events in the on-drug period (active and retreatment periods together).

5.6. General Adverse Events

The occurrence of all treatment-emergent adverse events (excluding infection and ISR), infections, infections considered preventable by vaccination, and injection site reactions will be separately summarized by incidence rate (proportion of subjects reporting events) and adjusted rate per 100 subject-years of exposure to etanercept. Adverse events will also be summarized by severity and relationship to investigational product. Adverse events occurring in >1 subject in any of the subtypes may be summarized as well.

- Tabulations of withdrawals from investigational product due to adverse events will be provided.
- In addition to showing cumulative rates over the entire study period (including both parent study and extension), incidences of subjects with treatment-emergent event as well as exposure-adjusted event rates will also be categorized by year for each year from 1 through 10.

These summaries will be performed for FAS (treatment-emergent events in on-drug period (active and retreatment periods together)) and WAS.

5.7. Laboratory, Vital Signs, Tanner Stage Assessment

For laboratory data, vital sign measurements and other continuous safety data, the number of observations, mean, standard deviation, median, minimum, maximum will be summarized by visit. Height, weight, BMI, and Tanner scores will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum by age group (ages 2-4, 5-11 and 12-17 years at start of parent study). The visits shown in these reports will be the baseline visit from the parent study, weeks 12, 24, 48, and 96, from the parent study and all visits from the extension study where

the data is collected. Some additional analyses of the Tanner data that takes age at time of measurement into account may also be done.

The Potentially Clinically Important (PCI) Flag is a derived flag value based on the PCI criteria defined for laboratory data captured in the study. The PCI criteria are based on NCI toxicity criteria. The number (%) of subjects with PCI events will also be provided for the lab data.

These summaries will be performed for FAS (active period (both parent and extension studies)), WAS, and RTAS.

5.8. Growth Parameters

Height, weight, and body mass index (BMI) will also be compared with data from standardized growth charts. Height, weight, and BMI will be summarized using Z-scores. Z-score is calculated using the following formulation:

$$Z = \frac{(X/M)^L - 1}{LS}, L \neq 0$$

Or

$$Z = \ln(X/M)/S, L = 0$$

where X is the physical measurement (eg, height, weight, BMI) and L, M, and S are the values from standardized growth charts provided by the US Centers for Disease Control website (http://www.cdc.gov/GrowthCharts/) by gender for children from birth to 240 months. The Z-score cannot be calculated if age > 240 months.

These summaries will be performed for FAS (active period (both parent and extension studies)), WAS and RTAS.

5.9. Efficacy Endpoints

Descriptive summary statistics will be provided for efficacy endpoints. For continuous endpoints, the summary statistics at each visit will include the number of observations, mean, standard deviation, median, minimum, maximum and 95% confidence interval for the mean. These statistics will be provided for the observed value and change from baseline. The mean percent change from baseline will be provided also. For categorical endpoints, the summary statistics will contain the frequency, percentage, and 95% confidence interval (CI) for the percentage.

These summaries will be performed for:

- FAS, active period data (both parent and extension studies. Baseline of parent study will be used for calculation of change from baseline). The reports will show the baseline (no baseline for ACRPedi responses), weeks 12, 24, 48, and 96 from the parent study and all visits from the extension study where data is collected.

- WAS. The reports will show all visits where data is collected.

- RTAS. Re-treatment period baseline will be used for calculation of change from baseline. The reports will show all visits where data is collected.

5.10. Health Outcomes Assessments

The CHAQ and HAQ will be summarized in the same way as the efficacy endpoints. CHAQ and HAQ results will be summarized separately.

5.11. Exposure

The exposure time (years) to etanercept will be calculated for each subject each period using (the last dose date – the first dose date + 1)/365.25. If the gap is less than 28 days between two etanercept treatment periods, the cumulative exposure will includes the gap. Otherwise, the gap will be excluded from the cumulative exposure. Descriptive statistics will be provided to summarize the exposure time for:

- FAS, on-drug period (active and re-treatment periods together);
- FAS, all periods (includes commercial etanercept in withdrawal and observational periods).

The total number of doses of investigational product taken will be summarized for FAS (active and re-treatment periods together).

A table showing the number of subjects taking investigational product for 1 year, 2 years and so on through 10 years may be provided for FAS (active and re-treatment periods together).

5.12. Nonstudy Medications

The number (%) of subjects using nonstudy medications will be reported by medication type (DMARD, NSAID, etc) for FAS (on-drug period (active and re-treatment periods together)) and WAS.

Separate tabulations will be provided for prior to, concomitant with or after investigational product will be provided for FAS (on-drug period (active and re-treatment periods together)).

5.13. Hospitalizations

Listings of subjects who are hospitalized will be provided for FAS.

5.14. Deaths

Listings of any deaths that occur will be provided for FAS.

The incidence of death may be compared to external data sources to generate standardized incidence ratios (SIRs) for:

- FAS, all periods;
- FAS, on-drug period (active and re-treatment periods together).

5.15. Data Monitoring Committee

This study will use an Internal Review Committee (IRC) to help assess the safety of the study. The IRC will be responsible for evaluation of periodic assessments of safety and efficacy data. A separate Charter will describe and govern the IRC's activity.

5.16. Data Derivation and Missing Data Handling

The following rules will be used to derive the endpoints and handle the missing components. If an endpoint is missing after derivation, the missing value will not be imputed.

5.16.1. Number of Active Joints

The active joints are defined as joints that are swollen or, in the absence of swelling, joints with limited range of motion accompanied by pain and/or tenderness. Total number of active joints is the number of active joints prorated for missing joints. It is defined as 73*(total number of active joints with score greater than zero)/number of non-missing active joints. Joint replacement (JR) and not evaluable (NE) are treated as missing. If more than 36 active joint scores are missing, then the total number of active joints will be defined as missing.

5.16.2. Number of Joints with Limited Range of Motion

Total number of joints with limited range of motion is the number of joints with limited range of motion prorated for missing limited range of motions. It is defined as 69*(total number of joints with score of limited range of motion greater than zero)/number of non-missing limited range of motions. Joint replacement (JR) and not evaluable (NE) are treated as missing. If more than 34 scores of limited range of motion are missing, then the total number of joints with limited range of motion will be defined as missing.

5.16.3. CHAQ/HAQ

For subjects < 18 years of age, the CHAQ will be used and completed by the subject's parent or legal representative/guardian. For subjects >= 18 years of age, he HAQ will be used and completed by the subject. CHAQ/HAQ contains eight domains: dressing, arising, eating, walking, hygiene, reach, grip, and common activities. Each item within a domain is scored on a 4-point Likert scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Not applicable is defined as missing. The highest score reported for a domain determines the score for that domain. In addition, a series of questions about use of aids or devices or help (e.g a cane for walking) are asked for each subscales. If the subscale score, based on the ordinal response, is missing, 0 or 1, but at least one of the aids or devices or help is used, the score is set to 2. The overall CHAQ/HAQ is computed as the sum of domain scores and divided by the number of domains answered. If 3 or more domains are missing, CHAQ/HAQ is defined as missing.

5.16.4. ACR Pedi Response

Scoring algorithm including missing data handling for ACR Pedi 30, 50, 70, 90, and 100: First, if any of the components have a score of zero at baseline and the post baseline score is >0, that component will be treated as worsening >30% for scoring improvement; if the baseline score is 0 and the post baseline score is also zero, improvement will be set to 0%. Then the algorithm described in the table below will be applied, based on the number of components with worsening >30%, missing, and improvement >30% (or 50% for ACR Pedi 50, etc).

Worsening>=30%	Missing	Improvement>30%	Outcome
>=2			Non-responder
1	0	>=3	Responder
		<3	Non-responder
	1	>=2	Missing
		<2	Non-responder
	2	>=1	Missing
		0	Non-responder
	>=3		Missing
0	0	>=3	Responder
		<3	Non-responder
	1	>=3	Responder
		2	Missing
		<2	Non-responder
	>=2		Missing

5.16.5. Juvenile Arthritis Disease Activity Score (JADAS)

JADAS consists of four components: physician global assessment of disease activity on a 10 cm VAS (0=no activity, 10=maximum activity); parent/patient global assessment of well-being on a 10 cm VAS (0=very well, 10=very poor); number of joints with active disease; and an inflammatory marker CRP. CRP was truncated to a 0–10 scale according to the following formula:

$$(\text{CRP (mg/l)} - 10)/10,$$

Before calculation, CRP values <10 mg/l were converted to 10 and CRP values >110 mg/l were converted to 110. JADAS was calculated as the simple linear sum of its four components. If one or more components are missing, JADAS score will be missing.

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