26 April 2019
EMA/191269/2019
Human Medicines Evaluation Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Orencia

abatacept

Procedure no: EMEA/H/C/000701/P46/063

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction

On 29 January 2019, the MAH submitted a clinical study report and a clinical study report addendum related to a completed paediatric study (study number IM101365) for ORENCIA, in accordance with Article 46 of Regulation (EC) No 1901/2006, as amended.

The MAH had issued a CSR for study IM101365 in December 2016 to support a supplemental Japanese New Drug Application in Juvenile Idiopathic Arthritis (JIA); the CSR summarised results based on a 1-year data cut-off (52 weeks from last patient first treatment) up to a database lock in September 2016. The study continued after the September 2016 database lock and was closed on 30 July 2018. A CSR addendum was prepared, summarising the results during the cumulative period up to the July 2018 database lock. The current submission includes both CSR's [Study IM101365 CSR (1-year data cutoff - September 2016 database lock); Study IM101365 CSR addendum (cumulative period - July 2018 database lock)].

A clinical expert overview, summarising the results of the study, was also provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study number IM101365, entitled "A Phase III, Multicenter, Open-Label Study to Assess Efficacy, Safety, Pharmacokinetics and Immunogenicity of Abatacept Administered Intravenously in Japanese Children and Adolescents with Active Juvenile Idiopathic Arthritis Who Have a History of an Inadequate Response or Intolerance to Methotrexate or Biologics" is a stand alone study.

The MAH stated that, in accordance with Article 16(2) of Regulation (EC) No 726/2004, the data submitted do not influence the benefit-risk balance for ORENCIA and therefore do not require further regulatory action to be taken on the marketing authorisation for this product.

2.2. Information on the pharmaceutical formulation used in the study

The study product was Abatacept for IV infusion, 250 mg/vial. Before use, the product was reconstituted with 10 mL of sterile water for injection or normal saline.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted two clinical study reports for study IM101365, entitled "A Phase III, Multicenter, Open-Label Study to Assess Efficacy, Safety, Pharmacokinetics and Immunogenicity of Abatacept Administered Intravenously in Japanese Children and Adolescents with Active Juvenile Idiopathic Arthritis Who Have a History of an Inadequate Response or Intolerance to Methotrexate or Biologics":

- CSR issued 29 December 2016 (1-year data cutoff - September 2016 database lock)
- CSR addendum issued 27 December 2018 (cumulative period - July 2018 database lock)

2.3.2. Clinical study

Study IM101365

Description

Study IM11365 was a Phase 3 non-comparative (single arm), open label, multicenter study to evaluate the efficacy, safety, pharmacokinetics and immunogenicity of IV abatacept in Japanese children and adolescents with active JIA and a history of an inadequate response or intolerance to methotrexate (MTX) or biologics. The study comprised a 16-week short-term (ST) period, followed by a long-term (LT) period of variable duration.

Methods

Objective(s)

The primary objective was to assess the primary efficacy as assessed by American College of Rheumatology Pediatric (ACR Ped) 30 response rate at Week 16 (Day 113) in Japanese active JIA subjects.

Secondary objectives were to assess the following after the 16-week ST period:

- ACR Ped 50, ACR Ped 70, ACR Ped 90 response rates and inactive disease rate
- Physical function as measured by the disability index of the Childhood Health Assessment Questionnaire (CHAQ)
- Safety and tolerability
- Pharmacokinetics
- Immunogenicity

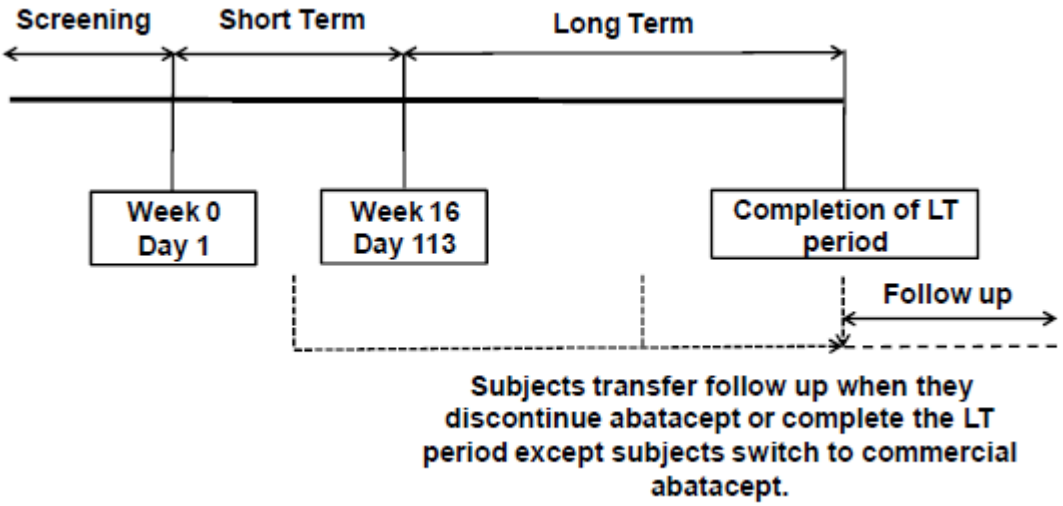
Exploratory objectives were to assess:

- ACR Ped 30, 50, 70, 90 response rates and the inactive disease rate in the ST + LT period of the study.
- Changes of the JIA Core Set Variables (ACR Pediatric components) in the ST + LT period of the study.
- Remission rate, minimal disease activity rate and the change from baseline in disease activity as measured by the Juvenile Arthritis Disease Activity Score 27 (JADAS27)-CRP in the ST + LT period of the study.
- Long-term safety in the ST + LT period of the study.
- Immunogenicity during the ST and LT period and up to 6 months following discontinuation of treatment.
- The generation and impact of anti-glutamic acid decarboxylase (GAD) and anti-thyroperoxidase (TPO) auto-antibodies and thyroid stimulating hormone (TSH) prior to, during the ST and LT period and up to 6 months following discontinuation of treatment.

Study design

The study was a non-comparative, open label study, comprising a screening period, a 16 week short-term (ST) period, followed by a long-term (LT) period that was to end when the product was approved in Japan (hence the variable duration of the LT period). See Figure 1 for a graphical depiction.

Figure 1. Study design



In the ST period, IV abatacept was to be administered as combination therapy with MTX or as monotherapy. The dose of MTX was to be stable in the ST period. After completion of the ST period, subjects were to enter the LT period automatically and continue to receive open-label IV abatacept until IV abatacept is approved for the indication of JIA or until the MAH elects to terminate development for the indication of JIA. During the ST and the LT period, non-biologic DMARDs (except MTX) and biologics were prohibited; minimum wash-out for biologics was 5 terminal half-lives before first dose of study medication. Stable low doses of oral corticosteroids and NSAIDs (oral formulations and rectal suppositories) were permitted in the ST period.

Subjects who discontinued abatacept prematurely in the ST or LT period, or completed the LT period, were to have follow-up visits at 28, 84 and 168 days after the last dose of study drug. If a subject started commercial abatacept after completion of the LT period, the follow-up period was considered completed at the start of commercial abatacept; subjects switching to commercial abatacept during the LT period were not permitted to enter the follow-up period.

According to the MAH, the study design was selected based on the efficacy of abatacept already having been demonstrated in a global JIA study (IM101033), whereby it was considered unethical to randomise subjects to placebo, as well as on local feasibility considerations. Its main aim was to compare results with the global study IM101033 and thus enable bridging between Japanese and non-Japanese patients. The study design was based on a formal consultation with the Japanese PMDA.

Study population /Sample size

Key inclusion criteria for subjects were:

- Male or female, age 4 to 17 years (inclusive) at enrolment.

- Diagnosis of JIA by International League of Associations for Rheumatology (ILAR) criteria of one of the following types: oligoarticular; polyarticular rheumatoid factor positive (RF+); polyarticular rheumatoid factor negative (RF-); or systemic with a polyarticular-course.
- A history of an inadequate therapeutic response or intolerance, in the opinion of the examining physician, to at least one biologic or MTX.
- A history of at least 5 joints with active disease and active articular disease at enrolment as defined by:
    - 2 or more active joints (e.g. presence of swelling, or if no swelling is present, limitation of motion (LOM) accompanied by pain, tenderness, or both) at screening and at Day 1 (Week 0).
    - 2 or more joints with LOM at screening and at Day 1 (Week 0).

  (The same joint could separately meet the definition of an active joint and a joint with LOM)

Key exclusion criteria were:

- Systemic onset JIA with any of the following manifestations within the last 6 months prior to enrolment: intermittent fever due to JIA, rheumatoid rash, hepatosplenomegaly, pleuritis, pericarditis, or macrophage activation syndrome.
- Presence of any other rheumatic disease or major chronic infectious/inflammatory/immunologic disease (e.g. inflammatory bowel disease, psoriatic arthritis, spondyloarthropathy, hypogammaglobulinemia, or systemic lupus erythematosus, etc.)

The planned number of subjects to be treated was 20. Of these 20 subjects, 3 subjects were to have a history of use of biologic therapies, and 5 subjects were to be treated with abatacept monotherapy in the ST period. The sample size was determined based on regional operational feasibility, and there was no formal statistical hypothesis for this study. In the global JIA study IM101033, ACR Ped 30 (CRP) response rate had been 63.7%, and based on an assumption of a 65% ACR Ped 30 response rate, the chosen sample size would provide a two sided exact 95% confidence interval (CI) of 40.8% to 84.6%.

Treatments

The dose of abatacept was based on weight at each study visit and tiered as follows:

- < 75 kg: 10 mg/kg
- 75 to 100 kg: 750 mg
- >100 kg: 1000 mg

Abatacept was administered on Day 1 (Week 0), Day 15 (Week 2), Day 29 (Week 4) and every 28 days thereafter for the duration of the study.

Outcomes/endpoints

The primary endpoint was the ACR Ped 30 response rate at Day 113. ACR Ped 30 response was defined as meeting both of the following:

- ≥ 30% improvement in at least 3 of the 6 JIA core set variables
- ≥ 30% worsening in no more than 1 of the 6 JIA core set variables

Secondary endpoints were:

- ACR Ped 50, 70, 90 response rates and inactive disease rate at Week 16 (Day 113)
- The disability index of the Childhood Health Assessment Questionnaire (CHAQ) at Week 16 (Day 113)
- Safety (proportion of subjects with AEs, deaths, SAEs, and AEs of special interest) during the ST period
- Pharmacokinetics (Cmax and Ctrough) during the ST period
- Immunogenicity positive rates during the ST period

Exploratory endpoints were:

- ACR Ped 30, 50, 70, 90 response rates and inactive disease rate, overall period (ST + LT period) of the study
- Changes from baseline of individual ACR pediatric components, including the disability index of the CHAQ, overall period (ST + LT period) of the study
- Remission rate, minimal disease activity rate and the change from baseline in disease activity as measured by JADAS27-CRP, overall period (ST + LT period) of the study
- Long-term safety summary (proportion of subjects with AEs, deaths, SAEs, and AEs of special interest), overall period (ST + LT period) of the study
- Immunogenicity positive rates during treatment and up to 6 months following discontinuation
- Assessment of anti-GAD and anti-TPO auto-antibodies and TSH during treatment and up to 6 months following discontinuation

Statistical Methods

The various response rates were computed with their respective two sided exact 95% CI. Summaries were provided for both the ST period and the cumulative period (ST + LT period) of the study. For the ST period analyses, an ACR non-responder status was imputed for prematurely discontinued subjects for all post-discontinuation visits up to Day 113. Analyses of the cumulative period were based on observed data.

All efficacy analyses were descriptive, and no formal statistical testing took place. CIs for proportions were computed using an exact method based on the binominal distribution.

CHMP comment:

It is understood that the study design and conduct were based on local considerations and needs; the study thus can be accepted as a supplementary, bridging piece of evidence within a global development program rather than a formal attempt to provide proof of efficacy or safety within a study. The global study IM101033 was a randomised withdrawal study and the design thus differs fundamentally from study IM101365; detailed comparison of results is therefore deemed beyond the scope of the current assessment.

Results

Recruitment / Number analysed

A total of 23 subjects were enrolled and 20 subjects were treated. Of the 20 subjects treated, 4 subjects had a history of biologics use, and 4 subjects were treated with abatacept monotherapy.

Baseline data

The age range of enrolled subjects was 5 - 16 years, and the majority were female. Mean duration of disease was 1.9 years, and most subjects had polyarticular JIA. Table 1 summarises the demographic characteristics, and Table 2 summarises baseline disease characteristics.

Table 1. Baseline demographic characteristics

	Abatacept N = 20
Age (years)	
Median (Min-Max)	10.5 (5-16)
Mean (SD)	10.2 (3.24)
Weight (kg)	
Median (Min-Max)	37.9 (15.4-68.3)
Mean (SD)	36.2 (14.9)
Gender (no., [%])	
Male	5 (25.0%)
Female	15 (75.0%)

Table 2. Baseline disease characteristics

	Abatacept N = 20
Duration of Disease (years)	
Mean (SD)	1.91 (2.682)
Median (Min, Max)	0.75 (0.2, 11.9)
Number of Active Joints	
Mean (SD)	7.1 (4.69)
Median (Min, Max)	6.0 (2, 19)
Number of Joints with limitation of motion	
Mean (SD)	4.1 (1.88)
Median (Min, Max)	4.0 (2, 10)
Parent Global Assessment (VAS 100mm)	
Mean (SD)	36.0 (25.34)
Median (Min, Max)	37.5 (0, 94)
Physician Global Assessment (VAS 100mm)	
Mean (SD)	41.8 (21.70)
Median (Min, Max)	37.0 (10, 80)
CHAQ disability Index	
Mean (SD)	0.763 (0.7411)
Median (Min, Max)	0.625 (0.00, 2.88)
CRP (mg/dL)	
Mean (SD)	0.856 (0.8763)
Median (Min, Max)	0.575 (0.02, 2.67)
JIA Disease Onset Category	
Extended Oligoarticular	2 (10.0%)
Polyarticular (RF -)	8 (40.0%)
Polyarticular (RF +)	10 (50.0%)
Systemic	0

Abbreviations: VAS = Visual analog scale, CHAQ = Childhood Health Assessment Questionnaire, CRP = C-reactive protein, JIA = Juvenile idiopathic arthritis, RF = Rheumatoid factor

CHMP comment:

The study population in study IM101365 is not entirely comparable to that in the global study IM101033; for example, the population in IM101365 was slightly younger (median age 10.5 years compared to 13 years in the global study), had a shorter disease history (mean duration 1.91 years compared to 4.4 years) and fewer joints with active disease (mean number of active joints: 7.1 vs. 16.2). Polyarticular disease types, either RF+ or RF-, were most common in both studies.

The differences notwithstanding, the recruited sample in itself can be considered representative of JIA for purposes of evaluation of safety and efficacy.

Efficacy results

Short-Term Period

At Day 113 (Week 16), 90% of subjects (18/20 subjects, exact 95% CI: 68.3, 98.8) met the ACR Ped 30 response criteria. The proportions of subjects meeting the other ACR Ped responder criteria are depicted in Table 3.

Table 3. Proportion of subjects meeting ARC Ped response criteria - Day 113

Visit			Abatacept N=20
Day 113	ACR PED 30	Number of subjects n/m (%) Exact 95% CI	18/20 (90.0%) (68.3, 98.8)
	ACR PED 50	Number of subjects n/m (%) Exact 95% CI	15/20 (75.0%) (50.9, 91.3)
	ACR PED 70	Number of subjects n/m (%) Exact 95% CI	14/20 (70.0%) (45.7, 88.1)
	ACR PED 90	Number of subjects n/m (%) Exact 95% CI	7/20 (35.0%) (15.4, 59.2)
	INACTIVE DISEASE	Number of subjects n/m (%) Exact 95% CI	5/20 (25.0%) (8.7, 49.1)

The median percent improvement in CHAQ-DI from baseline to Day 113 was 43%; median percent improvement in the Physician Global Assessment was 81%, and median percent improvement in the Parent Global Assessment was 57%.

Cumulative Period

In general, the response was maintained over longer periods of time; for illustrative purposes, the proportions of subjects meeting the various ACR Ped responder criteria at 12 months and approximately 26 months of follow-up are displayed in Tables 4 and 5.

Table 4. Proportion of subjects meeting ARC Ped response criteria - 12 months follow up

Visit			Abatacept N=20
Day 365	ACR PED 30	Number of subjects n/m (%) Exact 95% CI	16/18 (88.9%) (65.3, 98.6)
	ACR PED 50	Number of subjects n/m (%) Exact 95% CI	16/18 (88.9%) (65.3, 98.6)
	ACR PED 70	Number of subjects n/m (%) Exact 95% CI	15/18 (83.3%) (58.6, 96.4)
	ACR PED 90	Number of subjects n/m (%) Exact 95% CI	12/18 (66.7%) (41.0, 86.7)
	INACTIVE DISEASE	Number of subjects n/m (%) Exact 95% CI	8/18 (44.4%) (21.5, 69.2)

Table 5. Proportion of subjects meeting ARC Ped response criteria - 26 months follow up

Visit			Abatacept N=20
Day 785	ACR PED 30	Number of subjects n/m (%) Exact 95% CI	16/17 (94.1%) (71.3, 99.9)
	ACR PED 50	Number of subjects n/m (%) Exact 95% CI	15/17 (88.2%) (63.6, 98.5)
	ACR PED 70	Number of subjects n/m (%) Exact 95% CI	15/17 (88.2%) (63.6, 98.5)
	ACR PED 90	Number of subjects n/m (%) Exact 95% CI	14/17 (82.4%) (56.6, 96.2)
	INACTIVE DISEASE	Number of subjects n/m (%) Exact 95% CI	14/16 (87.5%) (61.7, 98.4)

Corresponding decreases were seen with JADAS27-CRP; at Month 12, 78% of subjects had minimal disease activity and 50% of subjects were in remission, and at Month 26, 94% of subjects had minimal disease activity and 75% of subjects were in remission.

Results consistent with maintenance of effect in the longer term were also seen on other exploratory endpoints; median percent improvements from baseline to Month 12 and Month 26 of follow-up were reported as 80% and 67% for CHAQ-DI, 97% and 100% for Physician Global Assessment, and 78% and 85% for Parent Global Assessment, respectively.

Safety results

Subject Disposition

Overall subject disposition is given in Table 6. Of the 4 subjects who discontinued during the LT period, the reasons for the discontinuation were subject request in 1 subject and lack of efficacy in 3 subjects. The subject who discontinued study medication due to her request did not wish to enter the follow-up period. Overall, 5 subjects (3 who had discontinued and 2 who had completed the LT period) entered the follow-up period and all 5 completed the follow-up period. A total of 14 subjects who completed the LT period did not enter the follow-up period because they were switched to commercial abatacept after the product was approved in Japan.

Table 6. Subject disposition

	Abatacept N = 20
Enrolled	23
Treated	20
Discontinued during Short-Term period	0
Completed Short-Term period	20
Discontinued during Long-Term period	4
Completed Long-Term period	16
Completed Long-Term period but did not enter follow-up period	14
Entered follow-up period	5
Discontinued during follow-up period	0
Completed follow-up period	5

Extent of Exposure

In the cumulative period, the median duration of exposure to IV abatacept was 42.1 months (range: 7-54 months), and the median number of abatacept infusions was 45 (range: 8-58).

Adverse Events

A summary of the adverse event data is presented in Table 7. In the cumulative period, all 20 subjects experienced at least one AE. AEs that occurred in 4 or more subjects were nasopharyngitis (17 subjects); pharyngitis (12 subjects); influenza (10 subjects); stomatitis, headache, and ligament sprain (7 subjects each); upper respiratory tract inflammation and contusion (6 subjects each); bronchitis, diarrhoea, acne, arthralgia and seasonal allergy (5 subjects each); gastroenteritis, upper respiratory tract infection, nausea and pyrexia (4 subjects each). Severe or very severe AEs were not reported in the cumulative period, except for a severe gastroenteritis in 1 subject (described below within section on SAEs). No deaths and no discontinuations due to an AE were reported.

Table 7. Summary of adverse events during the cumulative period

	Number (%) of Subjects Abatacept (N = 20)
	Cumulative period
Deaths	0
SAEs	6 (30.0)
Related SAEs	1 (5.0)
Discontinued due to AEs	0
AEs	20 (100)
Related AEs	6 (30.0)
AEs of special interest	-
Infections	20 (100)
Malignancies	0
Autoimmune disorders	3 (15.0)
Infusion reactions	-
Acute infusional AEs	1 (5.0)
Peri-infusional AEs	6 (30.0)
Other AEs within 24 hours	14 (70.0)

A total of 8 SAEs in 6 subjects were reported in the study (Table 8); among these, 2 SAEs in one subject were deemed related to study drug. These SAEs concerned two occurrences of acute gastroenteritis in one subject. The first episode, with onset on Day 21 and a duration of 3 days, was deemed mild. The second episode, with onset on Day 362 and a duration of 4 days, was deemed severe. No action with study medication was taken on either occasion.

Table 8. Serious adverse events reported in the study

ABATACEPT N=20

SYSTEM ORGAN CLASS (SOC) PREFERRED TERM (PT)	SUBJECTS WITH EVENT (%)
TOTAL SUBJECTS WITH AE	6 (30.0)
INFECTIONS AND INFESTATIONS	4 (20.0)
ENTEROCOLITIS VIRAL	1 (5.0)
GASTROENTERITIS	1 (5.0)
VARICELLA	1 (5.0)
VIRAL TONSILLITIS	1 (5.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	2 (10.0)
JUVENILE IDIOPATHIC ARTHRITIS	2 (10.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (5.0)
LOWER LIMB FRACTURE	1 (5.0)

The MAH defined infections, malignancies, autoimmune disorders, and infusion reactions as AEs of special interest (AESI) and assessed these through pre-specified MedDRA queries:

- Infections were reported in all 20 subjects in the cumulative period. The most common infections were nasopharyngitis in 17 subjects, followed by pharyngitis in 12 subjects and influenza in 10 subjects. Apart from the case of severe gastroenteritis (described above within section on SAEs), no other severe or very severe infections were reported in the cumulative period.
- No malignancies were reported in the study.
- In total, an autoimmune disorder was reported in 3 subjects during the cumulative period (alopecia areata in 1 subject and JIA in 2 subjects). Alopecia areata was mild in intensity and considered as unrelated to study medication.
- One acute infusional AE (i.e. an AESI occurring during the first hour after start of infusion) was reported. This was a case of mild pyrexia.
- Peri-infusional AEs (i.e. AESIs occurring during the first 24 hours after start of infusion) were reported in 6 subjects: nausea in 3 subjects; pyrexia in 2 subjects; injection site swelling and myalgia in 1 subject each. All of them were mild in intensity. Except for 1 case of nausea, the events were considered as unrelated to study medication.

The most frequently reported laboratory abnormalities were elevated eosinophil counts; mostly isolated occasions of elevated eosinophils were reported in 8 subjects overall.

During the cumulative period, 2 subjects converted from a negative anti-GAD status at baseline to a positive status, and 2 subjects converted from a negative anti-TPO status at baseline to a positive status. No subject had abnormal TSH values during the cumulative period.

Immunogenicity

During the cumulative period, a total of 4 subjects were determined as positive for antibodies to abatacept, CTLA4 and possibly Ig. Seropositivity was transient and of a low titer in 3 cases.

Abatacept concentrations greater than 1 ug/mL were present in the seropositive samples in 3 cases, and neutralising antibodies could therefore only be analysed for one subject.According to the MAH, the presence of anti-drug antibodies appeared to have no effect on PK, safety and efficacy of abatacept.

Pharmacokinetic results

Serum abatacept Ctrough and Cmax data was provided for the ST period. Geometric mean Ctrough levels of abatacept increased from Day 15 to Day 29 following the IV infusion of abatacept on Days 1 and 15, and then decreased on Day 57 following the IV infusion on Day 29 (Table 9). Geometric mean Ctrough levels appeared to be at steady state starting on Day 57 and were maintained above the target therapeutic Ctrough level of 10 µg/mL during the ST period; on Day 113, Ctrough level was above 10 µg/mL in 15 out of the 19 subjects included in the PK analysis population. In addition, geometric mean Cmax levels were relatively constant from Day 57 to 113 (Table 10).

Table 9. Summary Statistics of Ctrough (ug/mL) Values for Abatacept during the Short-term Period: PK Analysis Population

Statistic	Day 15	Day 29	Day 57	Day 85	Day 113
Geo. Mean [N]	25.50 [18]	38.64 [17]	17.24 [20]	16.79 [18]	15.56 [19]
%CV	27.61	29.08	36.63	40.01	36.61

Table 10. Summary Statistics of Cmax (ug/mL) Values for Abatacept during the Short-term Period: PK Analysis Population

Statistic	Day 57	Day 85	Day 113
Geo. Mean [N]	163.13 [20]	172.43 [20]	167.85 [20]
%CV	26.22	23.15	18.42

CHMP comment:

The efficacy results in this small study are in line with those previously reported for abatacept. Consistent with the small sample size, the confidence intervals for the point estimates are wide.

The safety results are also consistent with previous experience. Infectious events are dominant within the safety data, but this is not unexpected and should also be viewed in light of the long follow-up periods of several years in most cases. The nature of the reported SAEs was consistent with what would be expected in a corresponding general population, and SAEs were mostly deemed to be unrelated to study medication.

Based on the reported PK data, the achieved exposures were in line with expectations and comparable to those reported in the global study.

2.3.3. Discussion on clinical aspects

Both from an efficacy and a safety perspective, the results of this small study are consistent with previous experience and use of abatacept in the treatment of JIA. Although detailed comparisons are not possible due to the limited sample size in study IM101365, there seems to be no marked difference in the efficacy or safety profile of abatacept between a Japanese population vs. the global study that did not include Japanese subjects.

Based on the results of this small paediatric study, the MAH has proposed no changes to the product information. The MAH's view is supported. The overall benefit-risk profile of abatacept remains unchanged.

3. CHMP overall conclusion and recommendation

The data reported in this small study is generally consistent with other data reported for ORENCIA and does not change its general benefit-risk profile. No changes to the current product information are warranted.

☒ **Fulfilled:**

No regulatory action required.

4. Additional clarification requested

NA