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Human Medicines Evaluation Division

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

ILARIS

canakinumab

Procedure no: EMEA/H/C/001109/P46/052

Note

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

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1. Introduction

On 15 January, the MAH submitted a completed paediatric study for Ilaris, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that Study G1301 was an open-label, single-arm, efficacy and safety trial of 4 mg/kg canakinumab in Japanese patients with SJIA. Canakinumab was administered to patients every 4 weeks for at least 48 weeks. Two interim analyses were conducted at Week 28 and Week 48. The analysis at Week 28 was to support the SJIA registration dossier in Japan and analysis at week 48 supplemented the dossier with additional safety data.

In the EU, Ilaris (canakinumab) was first granted marketing authorization on 23 October 2009 (European Commission Decision). Since then, Ilaris is indicated for:

1. the treatment of the following autoinflammatory periodic fever syndromes in adults, adolescents and children aged 2 years and older:

- Cryopyrin-associated periodic syndromes (CAPS) including:
  - Muckle-Wells syndrome (MWS),
  - Neonatal-onset multisystem inflammatory disease (NOMID) / chronic infantile neurological, cutaneous, articular syndrome (CINCA),
  - Severe forms of familial cold autoinflammatory syndrome (FCAS) / familial cold urticaria (FCU) presenting with signs and symptoms beyond cold-induced urticarial skin rash.
- Tumour necrosis factor receptor associated periodic syndrome (TRAPS)
- Hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD)
- Familial Mediterranean fever (FMF), in combination with colchicine, if appropriate.

2. The treatment of active Still's disease including adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. Ilaris can be given as monotherapy or in combination with methotrexate;

3. The symptomatic treatment of adult patients with frequent GA attacks (at least 3 attacks in the previous 12 months) in whom NSAIDs and colchicine are contraindicated, are not tolerated, or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate.

Ilaris is registered as a powder to be dissolved and injected subcutaneously, i.e., the 150 mg powder for solution for injection and the 150 mg powder and solvent for solution for injection (convenient kit).

A new pharmaceutical form, the 150 mg/ml solution for injection presentation, has also been recently approved in the EU. Ilaris is administered via subcutaneous injection.

2.2. Information on the pharmaceutical formulation used in the study

Canakinumab solution for sc injection was provided in vials that contained 150 mg/mL canakinumab in a 1 mL solution.

The batch and formulation numbers of the test drug are presented in Table 9-1.

Table 9-1 Study medication formulation and batch numbers

Study drug and strength	Formulation control number	Batch number
Canakinumab 150 mg/1 mL	7008797	Y183 1214
	7008797	Y086 0714
	7008797	S0002
	7008797	S0003

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- **CACZ885G1301: An open-label, single-arm, active-treatment, efficacy and safety study of canakinumab (ACZ885) administered for at least 48 weeks in Japanese patients with Systemic Juvenile Idiopathic Arthritis (SJIA) (Final analysis)**

2.3.2. Clinical study

Clinical study number and title

CACZ885G1301: An open-label, single-arm, active-treatment, efficacy and safety study of canakinumab (ACZ885) administered for at least 48 weeks in Japanese patients with Systemic Juvenile Idiopathic Arthritis (SJIA) (Final analysis)

Description

Study CACZ885G1301 evaluated the efficacy and safety of canakinumab in Japanese patients with SJIA. It was a phase III study designed to provide efficacy and safety data for canakinumab administered for at least 48 weeks as subcutaneous (s.c.) injection every 4 weeks in Japanese patients with SJIA. Interim analysis data at Week 28 and Week 48 from this study supported a registration submission of canakinumab for the indication of SJIA in Japan. Beyond Week 48, the study allowed patients to continue canakinumab treatment until it was approved for SJIA in Japan and was commercially available for clinical use.

Methods

Objective(s)

The primary objective of this study was to evaluate the efficacy of canakinumab, defined as the proportion of patients who achieved a minimum adapted ACR pediatric (hereafter ACR ped) 30 criteria at Week 8 and the proportion of patients with canakinumab treatment who were able to taper corticosteroids successfully at Week 28.

Successful oral corticosteroids tapering was defined as meeting one of the following:

- Patients with prednisone equivalent dose of > 0.8 mg/kg/day at baseline were able to reduce their dose to ≤ 0.5 mg/kg/day.
- Patients with prednisone equivalent dose from ≥ 0.5 mg/kg/day and ≤ 0.8 mg/kg/day at baseline were able to reduce their dose by at least 0.3 mg/kg/day.
- Patients with any initial prednisone equivalent dose at baseline were able to reduce their dose to ≤ 0.2 mg/kg/day.
- Patients with prednisone equivalent dose of ≤ 0.2 mg/kg/day at baseline were able to reduce their dose with any reduction

AND maintaining a minimum aACR ped 30 criterion.

The study population consisted of male and female patients (≥ 2 to < 20 years of age) with a confirmed diagnosis of SJIA as per International League Against Rheumatism definition (Petty et al 2004) confirmed at least 3 months prior to enrollment with an onset of disease < 16 years of age. Active disease at the time of baseline defined as follows was needed :

- At least 2 joints with active arthritis (using ACR definition of active joint);
- Documented spiking, intermittent fever (body temperature > 38° C) for at least 1 day during the Screening Epoch and within 1 week before first canakinumab dose;

CRP > 30 mg/L (3 mg/dL) (normal range: < 10 mg/L (1 mg/dL))

Study design

Study G1301 was an open-label, single-arm, efficacy and safety trial of 4 mg/kg canakinumab in Japanese patients with SJIA. Canakinumab was administered to patients every 4 weeks for at least 48 weeks. Two interim analyses were conducted at Week 28 and Week 48. The analysis at Week 28 was to support the SJIA registration dossier in Japan and analysis at week 48 supplemented the dossier with additional safety data. Here is reported the final analysis conducted at the end of study.

Study population /Sample size

A total of 19 patients entered the study, of which 16 (84.2%) continued until the study ended. Three patients prematurely discontinued prior to Week 28. Three patients discontinued the study: two patients discontinued due to lack of efficacy and one patient discontinued due the AE (SJIA flare). For two patients discontinued treatment phase due to lack of efficacy, one patient had SJIA flare leading to discontinuation of study drug, but the patient was judged by the investigator “lack of efficacy” as the primary reason for discontinuing treatment phase.

All of the patients were Asian and the majority were female (n=13, 68.4%). The mean age was 9.9 years with 18 pediatric patients aged less than 18 years old and one patient with 19 years old of age. Few patients were 6 years old or younger (3 patients, 15.8%) while the remaining patients were >12 years old. The median weight was 30.1 kg (range, 10.9 to 52.3 kg).

The median age of SJIA disease onset was 3.0 years (range, 1 to 12 years). The median time from SJIA diagnosis to study entry was slightly less than 6 years (2153 days; range, 131 to 6302 days). The median number of active joints was 4 (range, 2 to 36) and the median number of joints with limitation of motion was 3 (range, 0 to 16). The median standardized CRP at baseline was 198.7 mg/L (range, 48.8 to 1311.4 mg/L). All patients were receiving concomitant oral corticosteroids therapy at baseline.

The mean (SD) oral prednisone equivalent dose was 0.31 (0.257) mg/kg/day and 73.7% (14/19) of the patients received > 0 to ≤ 0.4 mg/kg/day. 78.9% (15/19) of the patients had previously used tocilizumab for treatment of SJIA.

Treatments

Patients received canakinumab 4 mg/kg (maximum dose was 300 mg) administered subcutaneously every 4 weeks at the study center throughout the study. Study drug dose adjustment and/or interruptions were not permitted, with the exception of need due to changes in patient size/weight.

Outcomes/endpoints

Efficacy: Efficacy assessments consisted of the adapted ACR pediatric (a ACR ped) criteria, oral steroid tapering, flare events, inactive disease, and parent's or patient's assessment of pain based on the 0-100 mm visual analog scale (VAS) in the Child Health Assessment Questionnaire (CHAQ)©.

Adapted ACR Pediatric criteria:

The a ACR ped response variables are the following:

1. Physician's global assessment of disease activity on a 0-100 mm VAS
2. Parent's or patient's (if appropriate in age) global assessment of patient's overall well-being based upon the 0-100 mm VAS in the CHAQ
3. Functional ability: CHAQ disability score
4. Number of joints with active arthritis
5. Number of joints with limitation of motion
6. Laboratory measure of inflammation: CRP (mg/L)
7. Absence of intermittent fever due to SJIA during the preceding week

A ACR ped 30/50/70/90/100 criteria:

The a ACR ped 30/50/70/90/100 criteria are defined as meeting all of the following:

- Improvement from baseline of ≥ 30%, ≥ 50%, ≥ 70%, ≥ 90%, or 100%, respectively, in at least 3 of the first 6 response variables
- No intermittent fever (i.e. oral, rectal, or axillary body temperature > 38°C only for several hours during the day) in the preceding week (variable 7)
- No more than one variable 1-6 worsening by more than 30%

Oral steroid tapering:

Patients using concomitant corticosteroids at study entry reduced their corticosteroid dose to the lowest possible dose/discontinuation beginning at Week 8 until the end of study, if eligible.

Bioanalytics:

Pharmacokinetic assessments: Canakinumab concentrations were assessed in serum by competitive enzyme-linked immunosorbent assay (ELISA) with lower limit of quantification (LLOQ) at 100 ng/mL.

Pharmacodynamic assessments: Total interleukin-1beta (IL-1β) (sum of IL-1β free and bound to canakinumab) was analyzed in serum by competitive two ELISA methods based on commercial kits with LLOQ at 0.5 pg/mL or 0.299 pg/mL.

Immunogenicity: Anti-canakinumab antibodies concentrations were analyzed in serum by a bridging electrochemiluminescence immunoassay. Soluble protein biomarkers: IL-6 and IL-18 were measured with chemilluminescence enzyme immunoassay and enzyme immunoassay, respectively.

Safety: Safety assessments consisted of collecting all adverse events (AEs), serious adverse events (SAEs), with their severity and relationship to study drug and pregnancies (all females of child-bearing potential). They included the regular monitoring of hematology, clinical chemistry, and urinalysis; regular assessments of vital signs, physical condition, and body weight; electrocardiogram; clinical assessment of serositis, splenomegaly, hepatomegaly, and generalized lymphadenopathy attributable to SJIA; sonography of spleen and liver; and local tolerability at the subcutaneous injection site. Occurrence of biologic features of macrophage activation syndrome (MAS) such as hemorrhages, central nervous system dysfunction, hepatomegaly, serum fibrinogen level < 2.5 g/L, cytopenia, hypertriglyceridemia, decreased platelet count, increased aspartate aminotransferase (AST), and hyperferritinemia were carefully monitored and significant findings were recorded.

Statistical Methods

The co-primary efficacy variables were the proportion of patients who achieved a minimum a ACR ped 30 criteria at Week 8 and the proportion of patients who were able to taper oral corticosteroids successfully at Week 28. The analysis of the co-primary efficacy variables were based on the FAS. Successful oral steroid tapering was defined as meeting one of the following:

1. Patients with prednisone equivalent dose of > 0.8 mg/kg/day at baseline were able to reduce their dose to ≤ 0.5 mg/kg/day.
2. Patients with prednisone equivalent dose from ≥ 0.5 mg/kg/day and ≤ 0.8 mg/kg/day at baseline were able to reduce their dose by at least 0.3 mg/kg/day.
3. Patients with any initial prednisone equivalent dose at baseline were able to reduce their dose to ≤ 0.2 mg/kg/day.
4. Patients with prednisone equivalent dose of ≤ 0.2 mg/kg/day at baseline were able to reduce their dose with any reduction

AND maintaining a minimum a ACR 30 ped criterion.

Frequency tables with the number and percentage of patients achieving a minimum a ACR ped 30 criteria at Week 8 and patients able to taper oral corticosteroids successfully at Week 28 were provided. With a small number of patients in this study, the efficacy results were presented in a descriptive manner. Neither a statistical model nor a statistical hypothesis was defined. For secondary efficacy variables and safety variables, data were presented in a descriptive manner. Data summaries were presented for individual efficacy and safety parameters. Continuous variables were summarized by descriptive statistics and number of patients with non-missing data. Categorical variables were summarized by absolute frequencies and percentages. Efficacy analyses were based on the FAS and safety parameters on the Safety set, which both consisted of all patients who received at least one dose of study drug under this study protocol.

Two interim analyses (at Weeks 28 and 48) were planned and conducted during the study. In order to support the registration dossier in Japan, the efficacy and safety analyses up to Week 28 were performed after all patients completed the Week 28 assessment. The second analysis was performed at Week 48 to supplement the dossier with long-term safety data.

Results

Recruitment/ Number analysed/Baseline data

All of the patients were Asian and about 70% were female. The mean age was 9.9 years with half of the patients aged 6 to < 12 years (52.6%). The number of patients aged 6 or younger was small (3 patients, 15.8%). The median weight was 30.1 kg (range, 10.9 to 52.3 kg).

Efficacy and PK/PD results

- For both of the co-primary endpoints, this study showed clinical efficacy of canakinumab treatment in Japanese SJIA patients. All of the 19 patients (100%) achieved a minimum of a ACR ped 30 at Week 8 and 14 out of 19 patients (73.7%) achieved successful steroid tapering at Week 28. As to the a ACR ped 30 endpoint, the confounding effect of steroid on ACR response in 4 patients who received increased dose of oral steroid and/or steroid pulse due to SJIA flare should be considered; however, this would not impact on the overall conclusion that a treatment effect was seen in a high proportion of patients.
- Patients exhibited an early-onset ACR response during the 28 weeks of treatment; over 80% of patients achieved a ACR ped 30 or 70 at as early as Week 2 and a ACR ped 90 as early as week 4. The responses in a high proportion of patients were maintained through Week 28; the proportion of patients with a minimum a ACR ped 30 remained 100% at almost all time points, and a ACR ped 70, 90, and 100 were achieved by over 90%, 90%, and 50% of patients, respectively, from Week 12 through Week 28.
- The proportion of responders (patients with a minimum of a ACR ped 30) was 84.2% at Week 2 and increased to 94.7% at Week 4, 100% at Week 8, and remained 100% for most weeks through Week 156. The proportion of responders at end of study was 89.5%.
- The proportion of patients who achieved a ACR ped 70 was 84.2% at Week 2 and increased to 94.7% at Week 4, 100% at Week 8, and remained about 94% or more for most weeks from Week 12 to Week 156. The proportion of responders at end of study was 89.5%.
- The proportion of patients who achieved a ACR ped 90 was 63.2% at Week 2 and increased to 84.2% at Week 4, 89.5% at Week 8, and remained over 90% from Week 12 to Week 44. The response was maintained to Week 156 (83.3% to 100%). The proportion of responders at end of study was 84.2%.
- The proportion of patients that successfully tapered steroids increased over time from Week 12 (7/18, 38.9%) to Week 28 (14/16, 87.5%). The proportion of patients that successfully tapered steroids remained stable after Week 28, and the proportion remained at or above 80% for most weeks through Week 156. At end of study the proportion was 66.7%. The proportion of steroid free patients increased over time and was 12.5% (2/16) at Week 28, 31.3% (5/16) at Week 48, 68.8% (11/16) at Week 96 and 80.0% (4/5) at Week 144. At end of study the proportion of steroid free patients was 55.6% (10/18).
- Each of the seven components of the a ACR ped criteria showed improvements starting at as early as Day 3 or Week 2 and for the remainder of the 28 weeks of treatment. The same degree of improvement was sustained after Week 28 through Week 48 for all of the components:
    - The physician's global assessment of disease activity on a 0-100 mm VAS showed a clear decline in disease activity from baseline, with a mean change of −62.6 mm (−95.3%) at Week 28, −63.9 mm (−95.9%) at Week 48 and −61.4 mm (−88.9%) at end of study.

- The parent's or patient's global assessment of patient's overall well-being on a 0-100 mm VAS showed a clear improvement in overall well-being, with a mean change of −71.9 mm (−93.9%) at Week 28, −68.6 mm (−88.4%) at Week 48 and −68.1 mm (−86.9%) at end of study.
- The CHAQ disability score showed improvement at the first evaluation at Week 2, which increased over time. At Weeks 28 and 48, the median change from baseline in the score was −1.1 (−100%) showing a treatment effect that is approximately 5.8 times the MCID. At end of study the median change from baseline was −1.0 (−100%). The majority of patients (75.0%) showed an MCID improvement (defined as a decrease ≥ 0.19 from baseline) in the score at Weeks 28 and 48 and at end of study.
- The number of joints with active arthritis showed a clear decline, with a median change of −4.0 (−100%) at Weeks 28 and 48 and at end of study.
- The number of joints with limitation of motion showed a clear decline, with a median change of −2.0 (−100%) at Week 28, −2.5 (−100%) at Week 48 and −2.0 (−100%) at end of study.
- Standardized CRP showed a clear decline as early as Day 3 and remained decreased by over 90%, with a median percent change from baseline of −98.7% (−188.7 mg/L) at Week 28, −99.4% (−188.7 mg/L) at Week 48 and −98.5% (−180.0 mg/L) at end of study.
- Absence of intermittent fever due to SJIA was achieved in all patients from Week 4 through Week 164 for most weeks. There were 2 patients, one at Week 56 and 1 at Week 124 with intermittent fever. At end of study, absence of intermittent fever was achieved in all patients (19/19).

- The flare criteria were met for a total 3 patients during the first 48 weeks of treatment. One patient experienced a flare after oral steroid tapering was started. There were 3 additional patients with flare reported after Week 48.
- Inactive disease was achieved in 60% to 70% of the patients from Week 4 onwards.
- There was an increase in arithmetic mean serum canakinumab concentrations from Day 3 to Week 24. Arithmetic mean concentration was then maintained from Week 24 to end of study, indicating that the concentration reached steady state by the time of Week 24. No unexpected declines were observed in individual profiles of the serum canakinumab concentrations.
- As expected, an increase in total IL-1β levels was observed following canakinumab dosing, signifying the binding of IL-1β to canakinumab.
- Median decreases from baseline were seen in IL-6 levels (−99.1% at Week 2 and −98.4% at Week 48). The median decrease from baseline in IL-18 levels was −19.5% at Week 24, but due to the large variability, nothing definitive can be concluded at this level of analysis.

Safety results

The overall safety profile of canakinumab in this final analysis at end of study was consistent with the known canakinumab safety profile for the SJIA patient population and with previous canakinumab studies in SJIA.

The main safety findings are as follows:

- The median duration of exposure was 791 days. Approximately 84% of patients received study treatment for 96 weeks or more. The mean/median number of injections was 27.5/28.0.
- Treatment-emergent AEs were reported for all patients and the most frequently affected primary SOCs were infections and infestations (89.5%; primarily nasopharyngitis) and skin and subcutaneous tissue disorders (84.2%; with eczema and urticaria the most frequent PTs).
- No deaths occurred during the study.
- SAEs were reported for 10 (52.6%) patients and largely represented events associated with disease activity and infections. Two patients discontinued study drug during the 48 week treatment period, none of the SAEs after Week 48 led to premature discontinuation of study drug.
- SAEs of MAS were reported for 3 patients (preferred term, histiocytosis haematophagic). The events were adjudicated by the MASAC and the adjudication outcomes were: insufficient information for one event, unlikely MAS for one event and possible MAS for one event. Additionally, 2 cases with laboratory findings suggestive of potential MAS were adjudicated by the MASAC as having some clinical and/or laboratory features of MAS but with possible alternative explanation (unlikely MAS).
- Cumulative changes for hemoglobin, platelets, neutrophils, leukocytes, CRP, ferritin, and fibrinogen were consistent with the anti-inflammatory response to canakinumab therapy.
- Notable abnormalities for hemoglobin or leukocytes represented isolated findings. None of the findings required treatment interruption or were associated with clinically relevant events. Notable abnormalities for neutrophils or platelets were noted for one patient for each.
- One (5.3%) patient had newly occurring, notably high ALT of > 20 × ULN during the 48 week treatment period. The elevations were noted while the patient was experiencing an AE of SJIA flare (reported term) and serious Epstein-Barr virus infection; the values decreased to below the baseline level in a month. No patient had combined abnormalities involving ALT/AST with total bilirubin and/or alkaline phosphatase (Hy's Law) during the study.
- Nine (47.4%) patients had newly occurring clinically notable abnormalities in systolic BP, 10 patients (52.6%) had notable abnormalities in diastolic BP. Many of these notable BP abnormalities were transient or isolated events. Abnormalities occurring at more than 2 consecutive visits were seen for 1 patient with notably low systolic and diastolic BP and for 1 patient with notably low diastolic BP. The occurrence of low systolic and diastolic BP at 2 or more consecutive visits was not reported as an AE for either patient.
- Ten (52.6%) patients had newly occurring clinically notable abnormalities in pulse. Only one of these patients had notable abnormalities at more than 2 consecutive visits. No AEs of tachycardia or bradycardia were reported.
- Most of the patients had no tolerability reaction. Mild (Grade 1) local injection site reactions were reported for 3 (15.8%) patients.
- No anti-canakinumab antibodies were detected through end of study.

2.3.3. MAH´s Discussion on clinical aspects

In study CACZ885G1301, an open label-single-arm study, a strong treatment response to canakinumab 4mg/kg every 4 weeks was demonstrated in Japanese patients with active SJIA. The onset of action was rapid and observed as early as day 3. By Week 2 the majority of patients achieved

an ACR ped 90 and inactive disease status and maintained this level of response for the remainder of the study. Further, a majority of patients successfully tapered their corticosteroid dose, with the proportion of patients able to completely discontinue the corticosteroid increasing over time from 12.5% at Week 28 to 68.8% at Week 96.

The overall safety profile in the study was consistent with previous studies with no new safety signals observed. The frequency of AEs, including infections and other events of interest, reported during the course of the study was consistent with the known safety profile of canakinumab reported in previous studies and reflected in the SmPC.

As the efficacy and safety data were consistent with those of prior clinical studies, the favourable benefit-risk profile of Ilaris remains unchanged.

3. Rapporteur's overall conclusion and recommendation

The results of the finalized study G1301 showed the efficacy of canakinumab in inducing and maintaining a treatment response and symptom control in the evaluated Japanese patients with active SJIA. Results at end of study also showed a high proportion of steroid tapering possibility with treatment of canakinumab in SJIA patients.

Infections were the most frequently reported events during the study. Infections and infestations are already described in the SmPC of Canakinumab. SAEs were mostly associated with disease activity and infections. some patients presented abnormalities of liver enzymes; however, most of them were isolated events with no clinically significant impact on patient management.

The safety data from the final analysis showed no new safety findings compared to the known safety profile of canakinumab.

No changes to the SmPC were proposed. This is acceptable.

☒ Fulfilled:

No regulatory action required.

Annex. Line listing of all the studies included in the development program

Below is the list of the studies that are part of the clinical development of canakinumab in the treatment of Systemic Juvenile Idiopathic Arthritis. The results of all below mentioned studies have been submitted to the EMA either as part of former article 46 applications or as part of Type II variations (procedures EMEA/H/C/001109/II/0026 and EMEA/H/C/001109/II/0060 approved in August 2013 and in September 2018 respectively).

Study title	Study number	Date of completion
A multi-centre, open label, repeated dose range finding study to evaluate the safety, tolerability, immunogenicity, pharmacokinetics and efficacy of an anti-IL-1beta monoclonal antibody (ACZ885) given subcutaneously in pediatric subjects with active systemic juvenile idiopathic arthritis	CACZ885A2203	LPLV: 9-Mar-2010
A randomized, double-blind, placebo controlled, single-dose study to assess the initial efficacy of canakinumab (ACZ885) with respect to the adapted ACR Pediatric 30 criteria in patients with Systemic	CACZ885G2305	LPLV: 2-Dec-2010

Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations		
A randomized, double-blind, placebo controlled, withdrawal study of flare prevention of canakinumab (ACZ885) in patients with Systemic Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations	CACZ885G2301	LPLV:12-Sep-2011
An open-label extension study of canakinumab (ACZ885) in patients with Systemic Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations	CACZ885G2301E1	LPLV:10-Dec-2014
An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA))	CACZ885G2306	LPLV: 25-Sep-2017
An open-label, single-arm, active-treatment, efficacy and safety study of canakinumab (ACZ885) administered for at least 48 weeks in Japanese patients with systemic juvenile idiopathic arthritis (SJIA).	CACZ885G1301	LPLV: 01-Aug-2018