EMA/112036/2024
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

ILARIS

International non-proprietary name: Canakinumab

Procedure No. EMEA/H/C/001109/P46/059

Note

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

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1. Introduction

On 12 December 2023, the MAH submitted a completed paediatric study 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 CACZ885GBE01, a national, non-interventional retrospective/prospective registry of Systemic Juvenile Idiopathic Arthritis (SJIA) and Hereditary Periodic Fever Syndrome (HPFS) (Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D syndrome (HIDS)/ Mevalonate Kinase Deficiency (MKD), Familial Mediterranean Fever (FMF)) patients prescribed Ilaris (canakinumab) in Belgium, is a standalone study.

2.2. Information on the pharmaceutical formulation used in the study

Ilaris® (canakinumab) 150 mg powder for solution for injection (EU/1/09/564/001)

Ilaris® (canakinumab) 150 mg powder for solution for injection (EU/1/09/564/002)

Ilaris® (canakinumab) 150 mg/ml solution for injection (EU/1/09/564/004)

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- CACZ885GBE01, Belgian Registry of SJIA and HPFS (TRAPS, HIDS/MKD, FMF) patients treated with Ilaris® (canakinumab)

2.3.2. Clinical study

CACZ885GBE01, Belgian Registry of SJIA and HPFS (TRAPS, HIDS/MKD, FMF) patients treated with Ilaris® (canakinumab)

Description

This was a national, non-interventional retrospective/prospective registry of SJIA and HPFS (TRAPS, HIDS/MKD, FMF) patients prescribed Ilaris® (canakinumab) in Belgium. The registry is based on patient-level data obtained with a paper-based case report form (CRF). The observation period was between 1 July 2018 and 30 June 2023. The objective was to describe the treatment follow-up of patients with SJIA and HPFS (TRAPS, HIDS/MKD, FMF) treated with Ilaris® (canakinumab) following the Belgian reimbursement criteria.

Methods

Study participants

Patients eligible for inclusion in this registry had to meet the following inclusion criteria:

- SJIA and HPFS (TRAPS, HIDS/MKD, FMF) patients who agreed to participate and were willing and able to sign the informed consent (or parent's/legally authorized representative(s) written informed consent in case of pediatric patient).
- Adults, adolescents, and children (from 2 years of age) with SJIA or HPFS (TRAPS, HIDS/MKD, FMF) who granted reimbursement for and who were treated with Ilaris® (canakinumab).

The exclusion criteria were the following:

- Patients who did not fulfill all the inclusion criteria

Treatments

Ilaris® (canakinumab) 150 mg powder for solution for injection (EU/1/09/564/001)

Ilaris® (canakinumab) 150 mg powder for solution for injection (EU/1/09/564/002)

Ilaris® (canakinumab) 150 mg/ml solution for injection (EU/1/09/564/004)

Study Variables

A list of variables that were captured in the paper based CRF is provided in table 9-1. All variables apply for patients <18 years and ≥18 year.

Table 9-1 Variables of interest

Variable	Timing
Indication (SJIA, TRAPS, HIDS/MKD and FMF)	Baseline (part 1)
Date 1st reimbursement approval	Baseline (part 1)
Date of approval of reimbursement prolongation(s)	Upon time of reimbursement approvals (part 2)
Date of every Ilaris® (canakinumab) treatment administration	At baseline and upon every treatment
Year of birth	Baseline (part 1)
Weight	Upon every treatment (part 1 and part 2)
Number of vials administered	Upon every administration (part 1 and 2)
Confirmation of treatment continuation after initial 6-months reimbursement period	At the end of the 6 months initial reimbursement period or at time of discontinuation (part 1 or part 2)
Date of Ilaris® (canakinumab) treatment discontinuation and reasons why	At the time of discontinuation (part 1 and 2)

Randomisation and blinding (masking)

N/A

Statistical Methods

No formal hypothesis testing was performed. The sample size was estimated to be approximately 75 (all indications of SJIA, TRAPS, HIDS/MKD and FMF) in approximately 12 centers in Belgium. These estimations are based on epidemiological data, input of Belgian medical experts and in line with the MEA convention. As this is a descriptive registry, no statistical hypothesis testing and hence no sample size calculation are applicable.

Results

Participant flow and recruitment

Data from 96 patients were collected by 9 centers.

Baseline data

Data from 96 patients were collected by 9 centers. Seventy-nine-point-two (79.2) % of patients were diagnosed with FMF (79.2%), 7.3% were diagnosed with SJIA, 13.5% with TRAPS and 6.3% with HIDS/MKD.

At Ilaris® (canakinumab) treatment initiation, 87.5% of patients were adults (≥18 years) and 12,5% were < 18 years. The mean age at the first Ilaris® (canakinumab) administration was 34.55 (±1.526) years (range 3-67 years). Most patients were female (54.2%). For 60.2% of patients the bodyweight was not available. From the 39.7% for whom bodyweight was available, 14% of patients were < 40 kg and 86% were ≥ 40 kg.

Number analysed

Eighteen (18) patients (18.8%) discontinued Ilaris® (canakinumab) treatment during the observational period: 3 patients with SJIA, 4 patients with TRAPS and 11 patients with FMF. The main reason for discontinuation was a lack of efficacy (53.2%).

Efficacy results

The mean number of vials per patient was 41.7 (± 29.3). SJIA patient received the largest number of vials per patient.

A median dose of 1 vial (range 1.00 – 2.98) of 150 mg Ilaris® (canakinumab) was given per administration. Patients suffering from SJIA received a median of 2 vials per administrations. The mean dosing per administration per indication was 162.73 (±32.00) mg, 293.18 (±90.41) mg, 166.13 (±61.37) mg and 169.23 (±47.11) mg for respectively FMF, SJIA, TRAPS and HIDS/MKD patients. Due to the relatively low number of patients for whom bodyweight data are collected, (36 out of 96 patients), the data are too limited. The mean interval between 2 consecutive administrations was 34.79 (±27.27) days. The mean duration of Ilaris® (canakinumab) treatment in the observational period was 38.70 (±18.20) months. For the 18 patients who discontinued Ilaris® (canakinumab) treatment during the observation period, the mean treatment duration was 13.64 (±15.62) months.

Safety results

Safety monitoring and safety reporting, where there was a safety relevant result, was to be provided on an aggregate level only; no reporting on an individual case level was required. Relevant findings from the study report would be included in the periodic aggregated regulatory reports submitted to Health Authorities.

There were no adverse events (AEs) nor serious adverse events (SAEs) nor pregnancies reported in the CRFs of this registry.

Upon reconciliation of reported AEs and SAEs with the database of this NIS CACZ885GBE01, we noticed that for 10 patients, who discontinued Ilaris (canakinumab) treatment within the study duration, the reason for discontinuation as reported in the paper CRF was "lack of efficacy". For neither of these 10 patients, this was reported as an AE by the investigators to Novartis. The Novartis patient safety department reported these 10 cases within 24 hours of the reconciliation date. It concerns 6 adult FMF patients, 1 adult TRAPS patient and 3 SJIA patients from which 2 adults and 1 patient <18 years at the date of last administration.

There was no reported death during the observation period in this registry.

2.3.3. Discussion on clinical aspects

Retention time on Ilaris was rather long, with a mean of 38.70 (±18.20) months within the observation period of maximum 5 years. Only 18.8% of patients stopped treatment and only 10.4% stopped due to lack of efficacy (according to the investigators' judgement). *No efficacy data was collected in this registry.*

AS no adverse events, nor serious adverse events were reported in this registry by any of the study sites, there is no new safety signal identified by this registry.

3. CHMP overall conclusion and recommendation

The efficacy and safety results of the presented registry study in paediatric subjects do not alter the benefit risk balance.

Overall, the described safety findings are in line with the already known profile reflected in the SmPC.

☒ **Fulfilled:**

No regulatory action required.