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SCIENCE MEDICINES HEALTH

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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/P46/048

Note

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

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1. Introduction

On 27 May 2016 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 **CACZ885DBE02**

A multi-center, prospective, observational study to collect health related quality of life data for all Belgian CAPS patients, treated with Ilaris® and included in the international Ilaris® Registry

is a stand-alone study.

ILARIS® 150 mg powder for solution for injection was registered in EU/EEA on 23 October 2009 through the centralized procedure for the following indication:

"Ilaris is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents and children aged 4 years and older with bodyweight above 15 kg, 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."

An application (II/21) was submitted in June 2012 to extend the treatment of ILARIS® to the most severe CAPS patients, who include the patients aged 2 to <4 years with body weight 7.5 kg or above. In addition, Novartis proposed in the application to escalate the dose up to a maximum of 600 mg or to 8 mg/kg every 8 weeks for all patients who did not achieve or maintain satisfactory clinical response at the currently approved dose of 300 mg or 4 mg/kg every 8 weeks. Approval was granted in January 2013.

Another pharmaceutical form, ILARIS® 150 mg powder and solvent for solution for injection also referred as injection kit, was registered in EU/EEA on 16 September 2011 to provide the components required for reconstitution and administration of the approved lyophilized powder presentation; i.e., a water for injection vial, an injection syringe, a safety needle, two vial adapters and four cleansing swabs (PSUR11).

On 18 February 2013 and 26 August 2013 approval was granted in EU for Gouty Arthritis (GA) and for Systemic Juvenile Idiopathic Arthritis (SJIA) indications, respectively. In the current EU SmPC (Section 4.1), ILARIS® is currently indicated for:

1. The treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents and children aged 2 years and older with body weight of 7.5 kg or above, 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.

2. The treatment of active 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 gouty arthritis attacks (at least 3 attacks in the previous 12 months) in whom non-steroidal anti-inflammatory drugs (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.

This Belgian Quality of Life study was set-up to fulfill the request from the local Health Authorities in Belgium to collect Health related Quality of Life data on all Belgian patients included in the international Ilaris® Registry CACZ885D2401(Protocol CACZ885DBE02).

The international Ilaris® Registry CACZ885D2401 (β-Confident Clinical Outcomes and Safety: A registry Study of Ilaris® (canakinumab) patients) is an open-label, long-term, prospective, observational, multicenter study to monitor the safety and effectiveness of Ilaris® in CAPS patients. The purpose of this international observational study (registry) is to gather additional information with respect to long-term safety and effectiveness of Ilaris® used to treat patients with CAPS in routine clinical practice (Amended Protocol CACZ885D2401). The LPLV of this registry was on 19 December 2015 which was later than the completion of the local Belgian Quality of Life study which was on 3 December 2015 (Clinical Study Report CACZ885D2401).

The population of the Belgian Quality of Life study consisted of 3 adults and 1 adolescent (<18 years at the time of inclusion in this study).

2.2. Clinical aspects

2.2.1. Introduction

The MAH submitted a final report for:

- **CACZ885DBE02: Belgian Quality of Life study for Ilaris® CAPS patients**

A multi-center, prospective, observational study to collect health related quality of life data for all Belgian Cryopyrin Associated Periodic Syndrome (CAPS) patients, treated with Ilaris® and included in the international Ilaris® Registry (CACZ885D2401).

2.2.2. Clinical study

Clinical study number and title

CACZ885DBE02: Belgian Quality of Life study for Ilaris® CAPS patients

A multi-center, prospective, observational study to collect health related quality of life data for all Belgian Cryopyrin Associated Periodic Syndrome (CAPS) patients, treated with Ilaris® and included in the international Ilaris® Registry (CACZ885D2401).

Description

The Quality of Life study was an ancillary study to the international Ilaris® Registry. It was a multi-center, prospective, observational study.

Setting
In conformity with the international Ilaris® Registry, there were no required visits associated with the Quality of Life study. The treating physician or other staff would ideally collect data in this Quality of Life study during routine clinical visits and during which the data collection in the international Ilaris® Registry was done. It was recommended to collect the quality of life data at the start of the Quality of Life study and every 12 months until study end.

Methods

Objective(s)

The objective of the Quality of Life study was to collect HRQoL data by use of the EUROQoL Five Dimension Questionnaire (EQ-5D) for all Belgian CAPS patients, treated with Ilaris® and included in the international Ilaris® Registry, on the request of the Belgian health authorities.

Study design

Multi-center, prospective, observational study

Study population /Sample size

The population, included in the Quality of Life study consisted of 4 of the 5 Belgian CAPS patients treated with Ilaris® and included in the international Ilaris® Registry. For the one patient who was included in the international Ilaris® Registry and not in this Quality of Life study, the parents did not give consent for the participation of their child in the Quality of Life study. The population consists of 3 adults and **1 adolescent** (<18 years at the time of inclusion in this study).

For patient demographics see the International Ilaris® registry (reported separately and subsequently to the present report).

No formal sample size calculation was done to manage enrolment in the Quality of Life study since the goal was to include all Belgian patients, included in the international Ilaris® Registry.

Variables and data sources

The data collected in the Quality of Life study were limited to the quality of life data captured through EQ-5D. All other patient data were collected in the international Ilaris® Registry.

Results

4 patients were included in this Belgian Quality of Life study. A total of 11 EQ-5D questionnaires were completed. EQ-5D questionnaires were collected on 2 timepoints for 2 patients, 3 timepoints for 1 patient and 4 timepoints for 1 patient. 2 patients completed EQ-5D questionnaires during Ilaris® treatment only. Both patients rated the 5 dimensions (mobility, self-care, activity, pain, anxiety) as “no problem” at all timepoints and had a health state of 11111 and an index score of 1. On the visual analogue score, both patients scored between 90 and 98. 2 patients completed EQ-5D questionnaires without Ilaris® treatment (before or after) as well as during Ilaris® treatment.

During Ilaris® treatment, one patient rated all 5 dimensions (mobility, self-care, activity, pain, anxiety) as “no problem” and had a health state of 11111 and a score index of 1. The other patient rated at one timepoint one dimension (pain) at “some problem” and had a health state of 11121 and an index score of 0,764. At another timepoint, she rated one dimension (pain) at “some problem” and she didn’t rate “activity” which was a missing value. She had a health state of 11921 and an index score of 0.916. On the visual analogue score, the 2 patients scored 88, 90 and 90 respectively. Without Ilaris® treatment, one patient rated 3 dimensions as “no problem” and 2 dimensions as “some problem” (activity, pain). The health state was 11221 and the index score was 0,733. The other patient rated 3 dimensions as “no problem” and 2 dimensions as “some problem” (pain, anxiety). The health state was 11122 and the index score was 0,661. On the visual analogue score, the 2 patients scored 65 and 80 respectively.

The rating “extreme problem” was not scored in any patient at any timepoint. This small number of patients and small number of EQ-5D collection timepoints and the variation in underlying Ilaris® treatment, makes it impossible to draw any conclusions from these results.

2.2.3. Discussion on clinical aspects

The HRQoL data were collected to fulfil the request from the local Health Authorities in Belgium for the revision of the Ilaris® reimbursement file in CAPS.

A total of 11 EQ-5D questionnaires were completed by 4 patients during the study. For 2 patients, all EQ-5D collections were on Ilaris® treatment for a total of 6 time points. 1 patient had 1 EQ-5D collection with Ilaris® treatment and 1 without (after) Ilaris® treatment and 1 patient had 1 EQ-5D collection without Ilaris® treatment (before) and 2 collections with Ilaris® treatment.

Due to this small number of patients and EQ-5D collection time points and due to this variation in underlying Ilaris® treatment, it is impossible to draw any conclusions concerning HRQoL patterns from these data.

The EQ-5D data collected in this Quality of Life study cannot be generalized neither to the Belgian CAPS patients, nor to the overall CAPS population, treated with Ilaris®.

3. Overall conclusion and recommendation

The report does not provide any new information regarding efficacy or safety of Ilaris treatment in CAPS patients. No conclusions can be drawn from the presented HRQoL data and therefore provides no evidence that further actions are required.

☒ Fulfilled:

No regulatory action required.