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Human Medicines Division

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

Cibinqo

Abrocitinib

Procedure no: EMEA/H/C/005452/P46/01152/1

Note

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

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Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	Start of procedure	25 February 2025	25 February 2025
☐	CHMP Rapporteur AR	31 March 2025	19 March 2025
☐	CHMP comments	14 April 2025	n/a
☐	Updated CHMP Rapporteur AR	16 April 2025	n/a
☒	CHMP outcome	25 April 2025	25 April 2025

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1. Introduction

On 10 February 2025, the MAH submitted a completed paediatric study for Cibinqo, 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 'Abrocitinib Expanded Access Protocol for the Treatment of Adolescents and Adults With Moderate to Severe Atopic Dermatitis' B7451064 is an expanded access study. Since the study was initiated in November 2020, abrocitinib has been approved in adults (December 2021) and adolescents (March 2024) with moderate-to-severe atopic dermatitis (AD) who are candidates for systemic therapy.

2.2. Information on the pharmaceutical formulation used in the study

During the study intervention period, abrocitinib was provided in bottles of open-label drug and administered orally at total daily doses of 100 mg QD (1 tablet) or 200 mg QD (2 tablets) based on the investigator's discretion.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- B7451064; Abrocitinib Expanded Access Protocol for the Treatment of Adolescents and Adults With Moderate to Severe Atopic Dermatitis

2.3.2. Clinical study

Study B7451064; Abrocitinib Expanded Access Protocol for the Treatment of Adolescents and Adults With Moderate to Severe Atopic Dermatitis

Description

This expanded access study provided access to abrocitinib until it became commercially available to patients who had inadequate treatment options due to inadequate response or intolerance to available approved medicated topical and systemic therapies, underlying conditions that precluded use of available approved medicated topical and systemic therapies, or lack of availability or access to approved medicated topical and systemic therapies and needed abrocitinib as a possible treatment regimen for moderate to severe AD.

This study was terminated for business reasons with correspondence sent to study sites in January 2024. The termination was not triggered by any emerging safety concerns or by a worsening of the benefit-risk ratio. For most participating regions (Austria, Belgium [adults only], Canada, Netherlands, Russia, Spain, Switzerland, Taiwan, and the US) abrocitinib became commercially available while the protocol was active with participants transitioning out of the protocol upon commercial availability of

drug. For participating regions of Australia and Belgium (adolescents only), abrocitinib was not commercially available for these participants at the time of protocol termination.

This was an open-label, non-comparative, multi-center, expanded access protocol of abrocitinib in adolescents and adults with moderate to severe AD who had inadequate options for treatment of their AD with available and approved medicated topical and systemic therapies. The study was conducted in countries where there was an intent to register abrocitinib for a marketing authorisation.

Methods

Study participants

This study enrolled participants with 12 years of age or older at the time of signing the informed consent who met all the following AD criteria:

- Clinical diagnosis of chronic AD (also known as atopic eczema) for at least 6 months prior to Day 1 and had confirmed AD at the Screening and baseline visits.
- Inadequate treatment options for moderate to severe AD due to history of inadequate response or intolerance to treatment with available approved medicated topical and systemic therapies for the treatment of AD, underlying conditions that precluded use of available approved medicated topical and systemic therapies for the treatment of AD, or lack of availability or access to approved medicated topical and systemic therapies for the treatment of AD.
- Moderate to severe AD as indicated by meeting at least 1 of the following on the day of the baseline visit:
    - IGA ≥3;
    - EASI ≥16.

Treatments

During the study intervention period, abrocitinib was provided in bottles of open-label drug and administered orally at total daily doses of 100 mg QD (1 tablet) or 200 mg QD (2 tablets) based on the investigator's discretion.

- Abrocitinib was administered QD beginning on Day 1. The Day 1 dose could be administered in the clinic following confirmation of eligibility or at home following the study visit.
- Participants and, as applicable, parents/legal guardians, were given clear dosing instructions to take either 1 tablet of abrocitinib QD (if assigned to 100 mg) or 2 tablets of abrocitinib QD (if assigned to 200 mg) by mouth with food at the same time each day whenever possible until instructed to stop or alter the dose by the investigator.

During study participation, the total daily dose of open-label abrocitinib could be adjusted between 100 mg or 200 mg at the discretion of the investigator. An investigator could temporarily interrupt dosing for up to a maximum of 30 days for a participant for safety reasons or while monitoring abnormal laboratory tests if the investigator judged that this was necessary.

The maximum total treatment duration for an individual participant could differ, as this was variable; a participant could continue to receive abrocitinib in this expanded access study until availability of commercial product in his/her country or until the sponsor terminated the study in that country.

Medicated and non-medicated topical treatments for AD were permitted throughout the study and were to be administered in accordance with local practice and regulations. After Week 4 if medically necessary, participants with intolerable AD symptoms could receive locally-approved rescue therapy with systemic corticosteroids for up to 14 days at a time, at the investigator's discretion, according to local product label. Concomitant treatments were defined as medications taken during study intervention and within 28 days after the last dose of study intervention. Prior medications for the primary diagnosis collected on the CRF included systemic treatments for AD taken during the participant's lifetime and non-systemic drug treatments for AD including topical treatments taken within 1 year of the baseline visit.

Objective(s)

The primary objective was to provide access to abrocitinib to adolescent and adult patients with or without background topical therapy who had inadequate treatment options due to inadequate response or intolerance to available approved medicated topical and systemic therapies, underlying conditions that precluded use of available approved medicated topical and systemic therapies, or lack of availability or access to approved medicated topical and systemic therapies and needed abrocitinib as a possible treatment regimen for moderate to severe AD.

The secondary objective was to gain additional safety and tolerability data for abrocitinib 100 mg and 200 mg QD with or without background topical therapy in adolescent and adult participants with moderate to severe AD in a 'real world' clinical setting.

The tertiary/exploratory objective was to gain additional efficacy data for abrocitinib 100 mg and 200 mg QD in different dose modification strategies with or without background therapy in adolescent and adult participants with moderate to severe AD in a 'real world' clinical setting.

Outcomes/endpoints

- Incidence of treatment-emergent AEs and SAEs.
- Incidence of SAEs and AEs leading to discontinuation.
- Incidence of serious infections, defined as any infection (viral, bacterial, and fungal) requiring hospitalisation or parenteral antimicrobials.
- % Change from baseline in the EASI total score at all scheduled time points.
- % Change from baseline in the percentage BSA affected at all scheduled time points.
- Change from baseline in the severity of PP-NRS at all scheduled time points.
- Change from baseline in POEM score at all scheduled time points.

Sample size

Due to the nature of this treatment access protocol, the number of participants to be enrolled was not predefined. The study plan accounted for enrollment and assignment to abrocitinib of approximately 500 participants with moderate to severe AD in the adolescent and adult population who could potentially benefit from abrocitinib therapy with or without medicated topical therapy.

A total of 390 participants were screened, of whom 12 participants were re-screened. A total of 316 participants were assigned to study intervention, of whom 312 participants were treated with abrocitinib. Of the 312 treated participants, 33 (10.6%) were adolescents of age ≥12 and <18 years.

Randomisation and blinding (masking)

N/A

Statistical Methods

No specific hypotheses were tested in this study. Descriptive summary statistics were provided for all endpoints.

Results

Participant flow

A total of 390 participants were screened, of whom 12 participants were re-screened. A total of 316 participants were assigned to study intervention, of whom 312 participants were treated with abrocitinib. 184 (59.0%) participants completed the study intervention phase of abrocitinib which was defined as a participant ending treatment phase participation due to commercial availability of abrocitinib. 128 (41.0%) participants discontinued the study intervention phase of abrocitinib with the most common discontinuation reasons being withdrawal by participant (35 [11.2%] participants) and AE (29 [9.3%] participants). 309 (99.0%) participants had follow-up status collected, and 215 (68.9%) participants completed follow-up.

Baseline data

Demographic and baseline disease characteristics are summarise below:

- The mean (SD) age was 38.0 (18.47) years.
- 33 subjects were adolescents ≥12 and <18 years.
- Most participants were White (217 [69.6%] participants).
- The mean (SD) EASI Total Score was 22.35 (12.727) at baseline.
- The mean (SD) %BSA was 34.37% (21.403%) at baseline.
- The mean (SD) PP-NRS was 7.4 (2.02) at baseline.
- The mean (SD) POEM was 20.1 (5.64) at baseline.
- All treated participants had moderate IGA (198 [63.5%] participants) or severe IGA (114 [36.5%] participants) at baseline.

Number analysed

Safety Analysis Set included 312 participants who received at least 1 dose of study intervention.

Efficacy results

There were no primary or secondary endpoints related to efficacy in this study and no separate analysis in adolescents was made.

<u>Percent Change From Baseline in the EASI Total Score at All Scheduled Time Points</u>

- The mean (SD) observed EASI Total Score of 312 treated participants was 22.35 (12.727) at baseline.
- 41 participants had an observed EASI Total Score at Week 96 with the mean (SD) observed EASI Total Score of 4.62 (6.784) and mean (SD) percent change from baseline of -69.26% (78.677%).

Percent Change From Baseline in the %BSA Affected at All Scheduled Time Points

- The mean (SD) %BSA observed values of 312 treated participants was 34.37% (21.403%) at baseline.
- Of 41 participants with available %BSA data at Week 96, the mean (SD) observed values of %BSA was 8.77% (13.733%) and the mean (SD) percent change from baseline was -68.91% (62.865%).

Change From Baseline in the Severity of PP-NRS at All Scheduled Time Points

- The mean (SD) PP-NRS observed values of 312 treated participants was 7.4 (2.02) at baseline.
- Of 41 participants with available PP-NRS data at Week 96, the mean (SD) observed values of PP-NRS was 3.2 (2.77) and the mean (SD) change from baseline was -4.2 (3.66).

Change From Baseline in POEM Score at All Scheduled Time Points

- The mean (SD) POEM observed values of 312 treated participants was 20.1 (5.64) at baseline.
- Of 41 participants with available POEM data at Week 96, the mean (SD) observed values of POEM was 9.5 (7.79) and the mean (SD) change from baseline was -10.6 (9.96).

Safety results

Treatment-Emergent AEs

A total of 244 (78.2%) participants experienced all-causality TEAEs, of whom 123 had treatment-related TEAEs. The most frequently reported all-causality TEAEs were COVID-19 (52 [16.7%] participants), Nausea (48 [15.4%] participants) and Dermatitis atopic (41 [13.1%] participants).

The most frequently reported treatment-related TEAEs were Nausea (36 [11.5%] participants) and Acne (23 [7.4%] participants).

Of the 33 participants with the baseline age of ≥12 and <18 years, 24 (72.7%) participants experienced all-causality TEAEs, of whom 7 had treatment-related TEAEs.

The most frequently reported all-causality TEAEs were Dermatitis atopic (6 [18.2%] participants) and Nausea (5 [15.2%] participants).

The reported treatment-related TEAEs included Abdominal pain, Nausea, Fatigue, Hypertransaminasaemia, Herpes simplex, Nasopharyngitis, Headache, Acne and Dermatitis atopic. No treatment-related TEAEs were reported in more than 2 participants.

Treatment-Emergent SAEs

A total of 17 (5.4%) participants experienced all-causality SAEs, of whom 5 had treatment-related SAEs.

No treatment-emergent SAEs were reported in more than 1 participant.

There was 1 SAE of Type 1 diabetes mellitus reported in an adolescent participant with age of ≥12 and <18 years at the date of SAE onset (15 years).

8 treatment-related treatment-emergent SAEs (Thrombocytopenia, Hypertensive heart disease, Duodenal ulcer, Ophthalmic herpes zoster, Renal abscess, Urosepsis, Cerebral venous thrombosis and Pulmonary embolism) were reported in 5 participants, with each SAE reported in a single participant.

Deaths

Two deaths were reported in this study.

A male participant aged 72 years experienced a severe SAE of COVID-19 on Study Day 96 which resulted in study intervention interruption. This participant experienced another 4 severe SAEs of Acute respiratory distress syndrome, COVID-19 pneumonia, Dyspnoea and Pulmonary oedema on Study Day 125. All these SAEs were due to exposure to COVID-19 virus and were not related to the study intervention as assessed by the investigator. This participant died due to COVID-19 pneumonia on Study Day 137.

A male participant aged 62 years experienced a severe SAE Hypertensive heart disease leading to death on Study Day 438, and this SAE was related to study intervention as assessed by the investigator.

No deaths were reported in the adolescent participants with baseline age of ≥12 and <18 years.

Serious Infections

A total of 4 (1.3%) participants in this study experienced treatment-emergent serious infections. No serious infections were reported in the adolescent participants with baseline age of ≥12 and <18 years.

Abrocitinib 100 mg QD and 200 mg QD were well tolerated in adult and adolescent participants with moderate to severe AD. No new safety signals were identified in this study.

2.3.3. Discussion on clinical aspects

Among adolescents between ≥12 to <18 years, 60.6% were male. BMI was lower than in adults, EASI score and median PP-NRS were similar to scores in adult participants.

For efficacy results, no subgroup analyses in adolescents are available. 33 adolescents aged 12-18 were included in the study (10.3% of total study population). For the parameters studied, all efficacy results showed better numbers (descriptive data only) after 96 weeks of treatment compared with baseline.

Regarding safety, 9 adolescents experienced mild TEAEs, 14 moderate and 1 subject experienced severe TEAEs. One serious adverse event was reported in one adolescent, type 1 diabetes mellitus. The subject was a 15-year-old male, receiving 200 mg abrocitinib. Day of onset was Day 583 of treatment; treatment was permanently stopped at Day 587. The causality was assessed as unrelated by the sponsor. Type 1 diabetes mellitus is not listed as a known adverse event, and based on mechanism of action, it is agreed that causality is probably unrelated. No further action is required.

Two deaths occurred during the study, both in males aged 62 and 72. One case was due to COVID-19 infection, and the other case was due to hypertensive heart disease. In the opinion of the investigator, there was a reasonable possibility that the event of hypertensive cardiovascular disease was related to the study drug. However, no deaths were reported in adolescents and the cases of death were both in older subjects with comorbidities and raise no further concern of safety in adolescents. No further action is required.

Treatment-emergent serious infections were reported in 4 (1.3%) subjects, none of them aged ≥12 to <18 years. Herpes infection and pneumonia are mentioned in SmPC section 4.8. No new safety issue is raised.

3. CHMP's overall conclusion and recommendation

Study B7451064 was an expanded access study. Since the study was initiated, abrocitinib has been approved for adults and adolescents with moderate to severe AD. The descriptive data from the study do not provide any new information regarding efficacy or safety in adolescents in addition to that already available and described in the product information of Cibinqo (abrocitinib).

☒ **Fulfilled:**

No regulatory action required.