25 January 2024
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Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Cibinqo

International non-proprietary name: Abrocitinib

Procedure No. EMEA/H/C/005452/P46/005

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**	**Need for discussion[2]**
☐	Start of procedure	27 Nov 2023	27 Nov 2023	☐
☐	CHMP Rapporteur Assessment Report	03 Jan 2024	21 Dec 2023	☐
☐	CHMP members comments	15 Jan 2024	n/a	☐
☐	Updated CHMP Rapporteur Assessment Report	18 Jan 2024	n/a	☐
☒	CHMP adoption of conclusions:	25 Jan 2024	25 Jan 2024	☐

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1. Introduction

On 13 November 2023, 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

Cibinqo which contains the JAK-inhibitor abrocitnib as active substance, was approved in EU on 09 December 2021 for the treatment of moderate-to-severe atopic dermatitis (AD) in adults who are candidates for systemic therapy.

The MAH stated that study '*a randomised, open-label, parallel-group study to evaluate the safety and efficacy of abrocitinib 100 mg and 200 mg tablets in participants aged 12 years and older with moderate to severe atopic dermatitis in India'* and number B7451094 is a stand-alone study. At present there is an ongoing Type II Variation to extend the indication to include adolescents (EMEA/H/C/005452/II/0010).

Worldwide, as of 18 September 2023, abrocitinib has received marketing authorisation in 79 countries.

The rational for the MAH to perform the study under evaluation is that 'per the Indian consensus statement for management of AD, patients with AD suffer from dry skin and defective skin barrier function, that manifests mainly as pruritus. Systemic therapy is used to treat patients with moderate to severe AD on failure of topical treatments. Currently approved systemic agents in India have modest efficacy in patients with moderate to severe AD but are associated with AEs that often limit long-term use.'

2.2. Information on the pharmaceutical formulation used in the study

The abrocitinib formulation currently marketed are 50 mg, 100 mg and 200 mg film-coated tablet.

Study intervention used in study B7451094 was abrocitinib 100 mg tablet, provided centrally by the sponsor.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study B7451094 'a randomised, open-label, parallel-group study to evaluate the safety and efficacy of abrocitinib 100 mg and 200 mg tablets in participants aged 12 years and older with moderate to severe atopic dermatitis in India'.

2.3.2. Clinical study

Study B7451094 - a randomised, open-label, parallel-group study to evaluate the safety and efficacy of abrocitinib 100 mg and 200 mg tablets in participants aged 12 years and older with moderate to severe atopic dermatitis in India

Description

Study objective and endpoints

The study objectives and endpoints of study B7451094 are presented below in the Table 1 below.

Table 1. Study objectives and endpoints

Type	Objective	Endpoints
Primary		
Safety	To evaluate the safety of abrocitinib in participants aged 12 years and older with moderate to severe AD.	• Incidence of AEs and SAEs.
Secondary		
Efficacy	To assess the efficacy of abrocitinib in participants aged 12 years and older with moderate to severe AD.	• Response based on IGA score of clear (0) or almost clear (1) and greater than or equal to 2 points improvement from baseline at Week 12. • Response based on achieving ≥75% improvement from baseline in the EASI total score (EASI-75) at Week 12. • Response based on ≥75% improvement from baseline in SCORAD (SCORAD75) at Week 12. • Change from baseline in POEM at Week 12 and at all scheduled time points. • Change from baseline in ADCT at Week 12 and at all scheduled timepoints.
Primary Sub-study		
	To evaluate the potential effects of abrocitinib on bone development in adolescent participants 12 to <18 years of age, as assessed by knee MRI.	• The proportion of bone safety findings in knee MRI 1 year after randomization in adolescent participants exposed to abrocitinib 100 mg and 200 mg QD.*

* This endpoint is only for the sub-study and was not analyzed at this main study, the final results will be presented in the supplemental CSR. The MRI results for adolescents at baseline are provided in this main CSR.

Methods

Study design

Study B7451094 was a randomised, open-label, parallel-group study to assess the safety and efficacy of orally administered tablets of abrocitinib 100 mg and 200 mg QD in participants aged 12 years and older with moderate to severe AD in India. A total of 200 participants were enrolled from 15 sites in India, and randomly assigned to study intervention. Safety endpoints were assessed throughout the entire study. Secondary efficacy assessments were conducted from Screening to end of treatment (EOT) visit.

Eligible participants must have met the eligibility criteria at baseline. Participants who met eligibility criteria at baseline underwent Day 1 assessments and were randomised in a 1:1 ratio to receive abrocitinib 200 mg QD or abrocitinib 100 mg QD in an open-label fashion.

In the main study, the total treatment period was 12 weeks. All participants underwent a 4-week off-treatment safety follow-up period thereafter. This study also included a sub-study evaluating whether abrocitinib had any potential effects on adolescent bone utilising knee MRIs. All adolescent participants 12 to <18 years of age are continuing to receive study intervention until 1 year after randomisation in the main study. The results of the sub-study will be included in the supplemental CSR for study B7451094.

Study participants

Enrolled in this study were participants with moderate to severe AD aged 12 years and older at the time of informed consent.

Demographics and baseline characteristics were generally balanced between the abrocitinib 100 mg and 200 mg groups.

Approximately half of the participants were female (109 participants, 54.5%). The median age of all enrolled participants was 33.0 years (range: 12.0 – 73.0 years). Median weight was 62.0 kg (range: 30.0 - 99.0 kg) and BMI was 24.0 kg/m^2 (range: 14.0 – 38.0 kg/m^2).

Table 2. Demographic characteristics – safety data set

	Abrocitinib 200 mg QD (N=99)	Abrocitinib 100 mg QD (N=101)	Total (N=200)
Age (years), n (%)			
<18	17 (17.2)	16 (15.8)	33 (16.5)
18-44	48 (48.5)	45 (44.6)	93 (46.5)
45-64	30 (30.3)	33 (32.7)	63 (31.5)
>=65	4 (4.0)	7 (6.9)	11 (5.5)
Median (range)	32.0 (12.0, 73.0)	36.0 (12.0, 73.0)	33.0 (12.0, 73.0)
Mean (SD)	35.4 (17.19)	37.5 (17.49)	36.4 (17.33)
Gender, n (%)			
Male	38 (38.4)	53 (52.5)	91 (45.5)
Female	61 (61.6)	48 (47.5)	109 (54.5)
Race, n (%)			
Asian	99 (100.0)	101 (100.0)	200 (100.0)
Ethnicity, n (%)			
Not Hispanic or Latino	99 (100.0)	101 (100.0)	200 (100.0)

Sample size

Out of the 235 screened participants, 200 participants were randomised and enrolled in this study: 101 participants received abrocitinib 100 mg QD and 99 participants received abrocitinib 200 mg QD, among whom 16 and 17 were adolescent participants who received abrocitinib 100 mg QD and 200 mg QD, respectively. As of the data cutoff date of 14 June 2023, a total of 153 participants (76.5%) (79 received abrocitinib 100 mg QD and 74 received abrocitinib 200 mg QD) completed the study treatment phase in the main study and entered the follow-up phase, with 151 (75.5%) participants completing the study follow-up. Thirty-two (16.0%) adolescent participants continued the study and entered sub-study.

Treatments

Orally administered study intervention, abrocitinib 100 mg tablet, were administered QD from Day 1 to Week 12. Participants were dispensed bottles of study intervention at Day 1, Week 2, Week 4 and Week 8 visits in the main study. Adolescents were dispensed bottles of study intervention during the main study and at Week 12, Week 24 and Week 36 visits in the sub-study. Participants were given clear dosing instructions to take either 1 tablet or 2 tablets of study intervention QD by mouth with meals. Participants swallowed the oral study intervention whole and did not manipulate or chew the medication prior to swallowing.

Statistical Methods and analysis set

The statistical methods were provided and found acceptable.

For safety analyses, participants were analysed according to the treatment they actually received (101 participants received abrocitinib 100 mg QD and 99 participants received abrocitinib 200 mg QD). For efficacy analyses, participants were analysed according to the treatment group they were randomised to (100 participants were randomized to abrocitinib 100 mg QD and 200 mg QD each) (ie, FAS).

Results

Effiacy results

The following is a summary of the efficacy results:

The proportion of participants who achieved IGA responses at Week 12 was comparable between abrocitinib 200 mg QD group and abrocitinib 100 mg QD group (48.5% vs 50.0%, respectively).

The proportion of participants who achieved EASI-75 responses at Week 12 was comparable between abrocitinib 200 mg QD group and abrocitinib 100 mg QD group (71.7% vs 69.0%, respectively).

The proportion of participants who achieved SCORAD-75 responses at Week 12 was slightly higher in abrocitinib 200 mg QD group (47.5%) compared to abrocitinib 100 mg QD group (43.0%).

Decreases (ie, improvement) from baseline in POEM total score were observed over time in both treatment groups, with the 200 mg QD group having the most marked reductions.

Decreases (ie, improvement) from baseline in ADCT total score were observed over time in both treatment groups, with the 200 mg QD group having the most marked reductions.

Safety results

Extent of exposure

Range and median exposure were comparable between treatment groups (median duration of treatment for both groups were 12.14 weeks). Most participants had 10 weeks or more of exposure. One participant (1.0%) in abrocitinib 200 mg QD group had actual dosing duration of <1 week.

Adverse events

The term "AE" refers to "TEAE" (treatment emergent adverse event) unless otherwise specified. AEs reported during the study are summarized below:

The proportion of participants with all-causality AEs was higher for the abrocitinib 200 mg QD group compared to abrocitinib 100 mg QD group (30.3% vs 25.7%). A similar trend was observed in the treatment-related TEAEs (18.2% vs 13.9%). An all-causality SAE (radius fracture) was reported in

1 adult participant in abrocitinib 100 mg QD group. Nine participants (4 in abrocitinib 100 mg QD group and 5 in abrocitinib 200 mg QD group) were temporarily discontinued from study intervention due to all-causality AEs. No medication error events were reported. No events of death were reported in the study.

- A total of 12 adolescent participants (12 to <18 years) experienced 19 AEs; 16 of the 19 events were mild in severity. Three events (nasopharyngitis, eczema herpeticum and varicella) were moderate in severity.

All-causality AEs were most frequently reported (in ≥10 participants in total) under the SOCs of Gastrointestinal Disorders, Skin and Subcutaneous Tissue Disorders, and Infections and Infestations. The most frequently reported all-causality TEAEs (in ≥2.0% participants in either treatment group) were gastrooesophageal reflux disease, nausea, vomiting, pyrexia, ALT increase, cough, dermatitis atopic and pruritus.

- The most frequently reported all-causality TEAE in adolescent participants was nasopharyngitis, which was reported in 3 adolescent participants in total.

There were 2 participants with AEs meeting the adjudication criteria, 1 of opportunistic infection and the other one of special interest infection. For 1 of the above 2 participants, an event was adjudicated twice with the same results. Both were adolescent participants.

Laboratory

The proportion of participants who had laboratory abnormalities (without regard to baseline abnormalities) was higher in the abrocitinib 200 mg QD group (64.2%) compared to that in the abrocitinib 100 mg QD group (53.6%).

Vital signs and electrocardiograms

No clinically meaningful findings in the vital signs measurements, ECGs, physical examination assessments, or other observations related to safety were observed in this study.

Knee MRI results

A total of 35 adolescents were enrolled in the sub-study (2 of the 35 participants were 17 years old at the time of screening based on year of birth only, however, the derived age was 18 years after applying month and day imputation to date of birth. Thus, there were 33 participants <18 years old. Knee MRI central radiology read at baseline was applied for these 35 participants. The results are summarized below:

- All 35 participants were evaluated via MRI scan of the knee for the presence of any finding(s) that would require subsequent adjudication (ie, any 'potential bone safety finding' or 'other finding'). Five participants (14.3%) had an MRI finding on central read that would require subsequent adjudication. There were no substantial differences in the proportion of participants with an MRI with one or more 'other finding' between treatment groups.
- Out of 35 participants evaluated, 5 (14.3%) had an MRI requiring adjudication, all with one or more 'Other finding' identified on the central MRI radiology: no participant (0%) had bone safety findings identified on independent adjudication; 4 participants (11.4%) had one or more 'other finding' identified on independent adjudication (2 had bone marrow edema signal, 2 had altered soft tissue fat signal).

MAH's overall conclusions

Study B7451094 was designed to assess the efficacy and safety of abrocitinib 100 mg and 200 mg QD in participants aged 12 years and older with moderate to severe AD in India. A total of 200 participants were enrolled, and the median duration of treatment *was* 12.14 weeks for both abrocitinib 100 mg and 200 mg group in the main study.

Efficacy

Abrocitinib 100 mg and 200 mg showed similar efficacy at Week 12 based on IGA responses, EASI-75 responses, and SCORAD-75 responses. Decreases (ie, improvement) from baseline in POEM and ADCT total scores over time, with the 200 mg QD group having the most marked reductions.

Safety

Abrocitinib was well tolerated. The observed safety events were consistent with those seen in other abrocitinib studies.

- The proportion of participants with both all-causality and treatment related TEAEs was higher for the abrocitinib 200 mg QD group compared to abrocitinib 100 mg QD group. *No events of death were reported in the study.* The proportion of participants who had laboratory abnormalities was higher in the abrocitinib 200 mg QD group compared to that in the abrocitinib 100 mg QD group.
- There were no adjudicated bone findings in the baseline (predose) knee MRI in participating adolescents.

Abrocitinib was determined to be safe and well tolerated. The safety was comparable to previous abrocitinib studies.

The submission of the safety and efficacy data from this study does not have any consequences for the EU marketing authorisation including the already currently approved EU SmPC for abrocitinib.

2.3.3. Discussion on clinical aspects

The results of the performed open-label study support the short-term clinical safety and efficacy of Cibinqo used in treatment of patients with AD in India. Data were also supportive of safety and clinical efficacy evaluated in 33 paediatric patients enrolled in the study. However, the total number of adolescents included in this study was small; thus, the interpretation of safety data in the adolescent group should be made with caution. The MRI substudy in adolescents is still ongoing.

The safety results were consistent with the currently documented safety profile of the product, as described in the label. The proportion of participants with both all-causality and treatment related TEAEs was higher for the abrocitinib 200 mg QD group compared to abrocitinib 100 mg QD group. The benefit-risk of abrocitinib is unchanged and no update to the Summary of Product Characteristics has been proposed based on these data, this is agreed by CHMP.

3. CHMP's overall conclusion and recommendation

No new findings on clinical efficacy and safety were observed in the performed post-marketing study B7451094. The MAH has not suggested any update to the product information based on the performed study, this is agreed by the CHMP.

☒ **Fulfilled:**

No regulatory action required.