9 November 2023
EMA/548309/2023
Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006, as amended

TAKHZYRO

Lanadelumab

Procedure No. EMEA/H/C/004806/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	11 Sep 2023	11 Sep 2023	☐
☐	CHMP Rapporteur Assessment Report	16 Oct 2023	22 Sep 2023	☐
☐	CHMP members comments	30 Oct 2023	n/a	☐
☐	Updated CHMP Rapporteur Assessment Report	06 Nov 2023	n/a	☐
☒	CHMP adoption of conclusions:	09 Nov 2023	09 Nov 2023	☐

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1. Introduction

On 02 June, the MAH submitted a completed paediatric study for Takhzyro, 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 ***SHP643-302***: *A Phase 3 Multi-center, Open-label Study to Evaluate the Efficacy and Safety of Lanadelumab (SHP643) in Japanese Subjects with Hereditary Angioedema* is a stand-alone study.

Of note, a procedure to extend the indication to children from the age of 2 years is currently under assessment in the EU (EMEA/H/C/004806/X/0034/G).

2.2. Clinical aspects

2.2.1. Introduction

The MAH submitted a final report for:

- ***SHP643-302***: *A Phase 3 Multi-center, Open-label Study to Evaluate the Efficacy and Safety of Lanadelumab (SHP643) in Japanese Subjects with Hereditary Angioedema*

2.2.2. Clinical study

Clinical study number and title

SHP643-302: *A Phase 3 Multi-center, Open-label Study to Evaluate the Efficacy and Safety of Lanadelumab (SHP643) in Japanese Subjects with Hereditary Angioedema*

Description

SHP643-302 was an open-label Phase 3 study planned to enrol approximately eight Japanese subjects, 12 years of age and older, with HAE Type I or II.

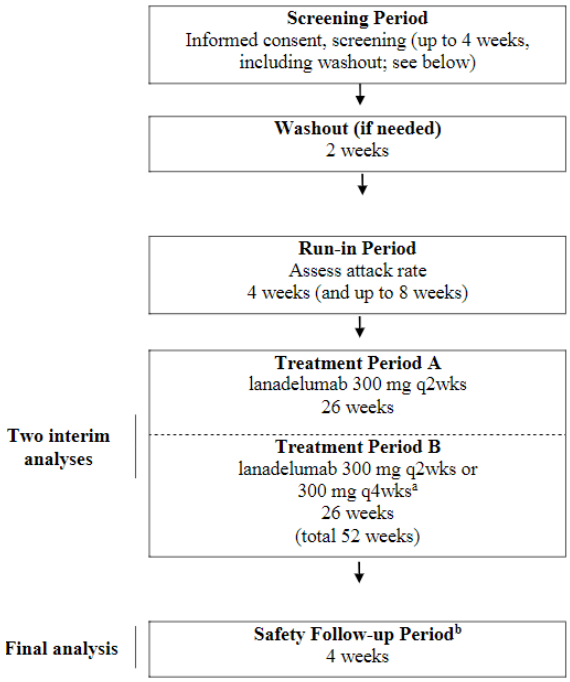
The study was intended to bridge the clinical data from global registration studies to Japanese HAE subjects; therefore, the study design for SHP643-302 was similar to that of the global pivotal study, DX-2930-03, with respect to readout of primary endpoint (26 weeks), dosing regimen (lanadelumab 300 mg q2wks), and efficacy outcome measures (e.g., reduction in HAE attacks).

Assessor's comment

Takhzyro was approved in the EU in 2018 (EMEA/H/C/4806) for *Routine prevention of recurrent attacks of hereditary angioedema (HAE) in patients aged 12 years and older.* Study DX-2930-03 is thoroughly described and assessed in that procedure.

Methods

Figure 1: SHP643-302 Study Design



Results

Recruitment

Eight subjects were recruited to the study. One subject (8.3%) was aged <18 years.

Baseline data

The age of onset of angioedema symptoms for the paediatric patient was <5 years. This subject experienced 27 attacks in the 12 months prior to screening and had an attack rate of 4.24 during the run-in period. The primary location of attacks was peripheral.

Efficacy results

The paediatric patient had no HAE attacks during the period of Day 0 through Day 182 (i.e., Treatment Period A). The subject switched to q4wks dosing in Treatment Period B and subsequently had 1 HAE attack corresponding to an attack rate of 0.08 per month for the period of Day 0 through Day 364 (i.e., the 52-week treatment period). The HAE attack was moderate in severity. The investigational medicinal product (IMP) dose was not changed in response to the attack.

Assessor's comment

There is no indication of lack of efficacy in the single subject < 18 years of age in Study SHP643-302.

Safety results

The paediatric patient had 5 non-HAE attack AEs during the overall treatment period (Day 0 through Day 364): 1 event of injection site swelling and 2 events of injection site reaction (all classified as

AESIs); 1 event of intercostal neuralgia; and 1 event under the System Organ Classes (SOC) Reproductive system and breast disorders.

The AEs of injection site swelling, and injection site reaction were all considered by the investigator to be related to the IMP. The other 2 AEs were considered to be not related to the IMP.

All of the AEs were mild in severity and were not reported as an SAE. All of the AEs resolved, and no action was taken with the IMP.

The subject also had 1 HAE attack AE during the overall treatment period. This event was moderate in severity and considered not related to the IMP. The event was not reported as an SAE and was not classified as an AESI. The event resolved and no action was taken with the IMP.

Assessor's comment

Injection site reactions are well-known adverse reactions to Takhzyro.

No new safety concerns were reported in the single subject < 18 years of age in Study SHP643-302.

2.2.3. Discussion on clinical aspects

One subject < 18 years of age was included in the Japanese Study SHP643-302 to bridge the clinical data from global registration studies to Japanese HAE subjects. Efficacy and safety in this subject were fully in line with the new profile for Takhzyro. No additional actions are considered needed.

3. CHMP's overall conclusion and recommendation

No additional actions are considered needed. The B/R for Takhzyro remains unchanged.

☒ **Fulfilled:**

No regulatory action required.