Amsterdam, 6 October 2025
EMADOC-1700519818-2423192
Committee for Medicinal Products for Human Use (CHMP)

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

Zeposia

Ozanimod

Procedure no: EMA/PAM/0000263324

Note

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

Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	26 May 2025	03 June 2025
☐	CHMP comments	10 June 2025	10 June 2025
☐	Updated CHMP Rapporteur AR	12 June 2025	12 June 2025
☐	Request for Supplementary Information (RSI)	19 June 2025	19 June 2025
☐	MAH replies to RSI	22 July 2025	9 July 2025
☐	Restart Date	23 July 2025	23 July 2025
☐	CHMP Rapporteur AR	6 August 2025	8 August 2025
☐	CHMP comments	11 August 2025	n/a
☐	Updated CHMP Rapporteur AR	14 August 2025	n/a
☒	CHMP Outcome	21 August 2025	21 August 2025

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1. Introduction

On 26 March 2025, the MAH submitted a completed paediatric study for Zeposia, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as part of the post-authorisation measure.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that Study IM047023 - *A Phase 2/3, Multicenter, Randomized, Double-Blind Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Oral Ozanimod (RPC1063) in Pediatric Participants with Moderately to Severely Active Crohn's Disease with an Inadequate Response to Conventional Therapy* - is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

As per the protocol, Ozanimod capsules, 0.23, 0.46, and 0.92 mg, developed for adults, will be administered in participants who can swallow the capsules. The adult capsule formulations, with a small capsule size (size 4) and closed dimensions of 14.3 mm length and 5.3 mm width, allow for ease of swallowing. Capsule excipients include the following compendial materials: microcrystalline cellulose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate. Capsule shells contain gelatin and colorants.

Participants were aged between 15 and 16 years of age, belonging to cohort 1. Therefore, all patients took ozanimod in the form of capsules.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study IM47023, Phase 2/3, Multicentre, Randomized, Double-Blind Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Oral Ozanimod (RPC1063) in Paediatric Participants with Moderately to Severely Active Crohn's Disease with an Inadequate Response to Conventional Therapy.

Ozanimod is an orally bioavailable bi-aryl oxadiazole small molecule that acts as a S1P receptor modulator, with 10-fold more selectivity for $S1P_1$ relative to $S1P_5$. Many cell types express $S1P_1$, including vascular endothelial cells, brain cells, and lymphocytes. Stimulation (agonism) of this receptor results in biological activities that include lymphocyte retention in peripheral lymphoid organs (e.g., lymph nodes and GI Peyer's patches), resulting in reversible systemic reduction in circulating lymphocytes. Given the immune-mediated inflammation in CD, prevention of circulation of disease-exacerbating, self-reactive lymphocytes to the gut is likely to have salutary immunomodulatory effects with a consequent dampening of disease processes.

Ozanimod is approved in the US, Europe, and other countries as a treatment for MS and UC.

2.3.2. Clinical study

Study IM047023

Description

This was a Phase 2/3, randomized, double-blind study to evaluate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics (PD) of oral ozanimod once daily at 2 dose levels (0.46 or 0.92 mg/day adult equivalent doses) in paediatric subjects aged 2 to 17 years, inclusive, with moderately to severely active Crohn's disease (CD) (defined as a paediatric Crohn's disease activity index [PCDAI] score of ≥ 30 and a simple endoscopic score for Crohn's disease [SES-CD] of ≥ 6 [or SES-CD ≥ 4 in subjects with isolated ileal disease]) with an inadequate response, intolerance, or loss of response to prior therapy for CD. The study planned to include a 64-week double-blind treatment period (12-week Induction Period and 52-week Maintenance Period) followed by an optional long-term extension (LTE) Period of up to approximately 4.5 years.

Additionally, the study had planned to evaluate PK and PD of oral ozanimod administered once daily at 2 dose levels (0.46 or 0.92 mg/day adult equivalent doses) in paediatric subjects during a 64-week Induction and Maintenance treatment period.

Bristol-Myers Squibb Company (BMS) decided to terminate the Study IM047023 as stated in the Dear Investigator Letter provided to sites on 03-Jun-2024. The decision to terminate the study was not related to any safety concerns or issues associated with the use of ozanimod; therefore, this clinical study report (CSR) is prepared in the synoptic format, and it also serves as a closeout CSR. At the time of study termination, 5 subjects were randomized and treated, but none of them reached Week 64 for the primary endpoints. The last patient last visit (LPLV) occurred on 13-Sep-2024.

The laws and regulatory requirements of all countries that had sites participating in this study were adhered to. This study was conducted in accordance with GCP, as defined by the International Council for Harmonization and in accordance with the ethical principles underlying European Regulation EU No. 536/2014.

Methods

Study participants

Approximately 120 paediatric subjects were planned to be enrolled and randomized sequentially across 3 age cohorts (Cohort 1: 12 to 17 years; Cohort 2: 6 to 11 years; Cohort 3: 2 to 5 years).

A total of 12 subjects were enrolled in the study. Of the enrolled subjects, 5 subjects were randomized and treated in Cohort 1: 3 subjects in 0.46 mg/day group and 2 subjects in 0.92 mg/day group. Seven of the 12 enrolled subjects were screen failures. Due to early termination of the study, Cohort 2 and Cohort 3 were never opened for enrolment.

Treatments

Ozanimod capsules 0.23, 0.46, and 0.92 mg, developed for adults were administered in subjects who could swallow the capsules and did not require a dose adjustment. Subjects underwent dose escalation over a minimum of 7 days. Cohort 1 initiated treatment with the same dose escalation schedule used

in adults across indications, as it had successfully attenuated the negative cardiac effects of S1P modulation in adults:

- **Ozanimod 0.46 mg/day dose:** 0.23 mg/day on Days 1 to 4, then 0.46 mg/day on Days 5 to 7, and continuing 0.46 mg/day from Day 8 forward
- **Ozanimod 0.92 mg/day dose:** 0.23 mg/day on Days 1 to 4, then 0.46 mg/day on Days 5 to 7, then 0.92 mg/day from Day 8 forward

For all cohorts, first dose monitoring (i.e., close cardiac monitoring for 6 hours post-first dose) and steady state PK data were to be evaluated to adjust the escalation regimen as required. The dose at which a subject entered the LTE Period was determined by their clinical response at the time of entry into the LTE Period.

Planned treatment duration included a 64-week double-blind treatment period (12-week Induction Period and 52-week Maintenance Period) followed by an optional LTE Period of up to approximately 4.5 years.

Objectives and Outcomes/endpoints

The following objectives and corresponding endpoints were planned in the protocol:

Table 4-1: Objectives and Endpoints

Objective	Endpoint
Primary – Efficacy	
• To evaluate the efficacy of ozanimod once daily in pediatric participants with moderately to severely active CD: clinical remission by PCDAI at Week 64	• Proportion of participants who achieve PCDAI < 10 at Week 64
• To evaluate endoscopic remission at Week 64 by SES-CD	• Proportion of participants achieving SES-CD ≤ 2 or SES-CD ≤ 4 points with no SES-CD subscore > 1 point at Week 64
Secondary – Efficacy (Key)	
• To evaluate the efficacy of ozanimod once daily in pediatric participants with moderately to severely active CD: clinical remission by PCDAI at Week 12	• Proportion of participants who achieve PCDAI < 10 at Week 12
Secondary – Efficacy (Other)	
• To evaluate endoscopic response by SES-CD	• Proportion of participants who achieve SES-CD decrease from Baseline of ≥ 50% (ER-50) at Week 64; Week 12
• To evaluate clinical response by PCDAI	• Proportion of participants who achieve reduction in PCDAI score ≥ 12.5 and a total PCDAI score of < 30 poi nts at Week 64; Week 12
• To evaluate symptomatic remission (adolescents only)	• Proportion of adolescents who achieve an average daily abdominal pain score ≤ 1 point and an average daily stool frequency ≤ 3 points with abdominal pain and stool frequency no worse than Baseline at Week 64; Week 12

• To evaluate change in CD symptoms over time	• Change from Baseline in stool frequency score over time • Change from Baseline in abdominal pain over time
• To evaluate clinical remission by CDAI (adolescents only)	• Proportion of adolescents who achieve CDAI score < 150 at Week 64; Week 12
• To evaluate clinical response by CDAI (adolescents only)	• Proportion of adolescents who achieve CDAI reduction from Baseline of ≥ 100 points or CDAI score < 150 at Week 64; Week 12
• To evaluate corticosteroid-free remission	• Proportion of participants who achieve a PCDAI score < 10 at Week 64 while remaining corticosteroid free in the prior 12 weeks • Proportion of participants who achieve a CDAI score < 150 at Week 64 while remaining corticosteroid free in the prior 12 weeks (adolescents only)
• To evaluate endoscopic remission at Week 12	• Proportion of participants achieving SES-CD ≤ 2 or SES-CD ≤ 4 points with no SES-CD subscore > 1 point at Week 12
Secondary –Pharmacokinetics	
• To characterize the PK of 2 doses of oral ozanimod and its major active metabolites in pediatric participants with moderately to severely active CD	• Steady state systemic exposures of ozanimod and CC112273 at Week 20 and throughout the study
Secondary –Pharmacodynamics	
• To evaluate the PD effects of 2 dose levels of ozanimod (eg, effects on ALC) in pediatric participants with moderately to severely active CD	• Absolute and percent change from Baseline in ALC at Week 64, Week 12, and throughout the study
Secondary – Safety and Tolerability	
• To evaluate the safety and tolerability of 2 dose levels of oral ozanimod once daily in pediatric participants with moderately to severely active CD	• Number and proportion of participants experiencing AEs, SAEs, AEs leading to discontinuation from treatment, and AESIs throughout the study
Abbreviations: AE, adverse event, AESI, adverse events of special interest; ALC, absolute lymphocyte count; AUC, area under the curve; BMI, body mass index; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; DXA, dual energy x-ray absorptiometry; ER-50, SES-CD decrease from Baseline of ≥ 50%; ET, early termination; GHAS, Global Histologic Activity Score; LTE, long-term extension; PCDAI, Paediatric Crohn's Disease Activity Index; PD, pharmacodynamics; PK, pharmacokinetics; RHI, Robarts Histopathology Index; SAE, serious adverse event; SARS-COV-2, severe acute respiratory syndrome coronavirus 2; SES-CD, Simple Endoscopic Score for Crohn's Disease; S1P1, sphingosine-1-phosphate receptor 1.	

CRITERIA FOR EVALUATION:

Efficacy:

Efficacy was measured by:

- Clinical remission (PCDAI < 10 points)
- Clinical response (PCDAI reduction from Baseline of ≥ 12.5 and a total PCDAI score of < 30 points)

- Endoscopic remission (SES-CD ≤ 2 or SES-CD ≤ 4 points and with no SES-CD subscore > 1 point)
- Endoscopic response (≥ 50% improvement from Baseline in the SES-CD)
- Symptomatic remission (average daily abdominal pain score ≤ 1 point and an average daily stool frequency ≤ 3 points with abdominal pain and stool frequency no worse than baseline)
- Change from baseline in stool frequency score and abdominal pain over time.
- Clinical remission by CDAI (CDAI score < 150)
- Clinical response by CDAI (CDAI reduction from baseline [Day 1 on dose] of ≥ 100 points or CDAI score < 150)

Efficacy endpoints were evaluated for all visits available.

Safety:

Safety measurements included AEs, SAEs, AEs leading to discontinuation from treatment, AESIs, deaths, laboratory assessments (outside of normal range results for haematology and chemistry, and abnormal liver function test results) and vital signs.

Pharmacodynamics:

PD evaluation included ALC and faecal calprotectin measurements.

STATISTICAL CONSIDERATIONS:

Due to the limited number of enrolments and the limited time for this study, only listings were produced and included in this synoptic CSR.

Efficacy:

Efficacy data were presented using the ITT population, unless otherwise specified.

PCDAI and its subscores and SES-CD and its subscores, and CDAI scores were listed for all visits for ITT population.

Safety:

Safety data were presented using the safety population. AEs were coded using MedDRA version 27.1.

Pharmacodynamics:

ALC and faecal calprotectin measurements were listed for safety population.

Sample size

Approximately 120 paediatric subjects were planned to be enrolled and randomized sequentially across 3 age cohorts (Cohort 1: 12 to 17 years; Cohort 2: 6 to 11 years; Cohort 3: 2 to 5 years).

A total of 12 subjects were enrolled in the study. Of the enrolled subjects, 5 subjects were randomized and treated in Cohort 1: 3 subjects in 0.46 mg/day group and 2 subjects in 0.92 mg/day group.

Seven of the 12 enrolled subjects were screen failures. Due to early termination of the study, Cohort 2 and Cohort 3 were never opened for enrolment.

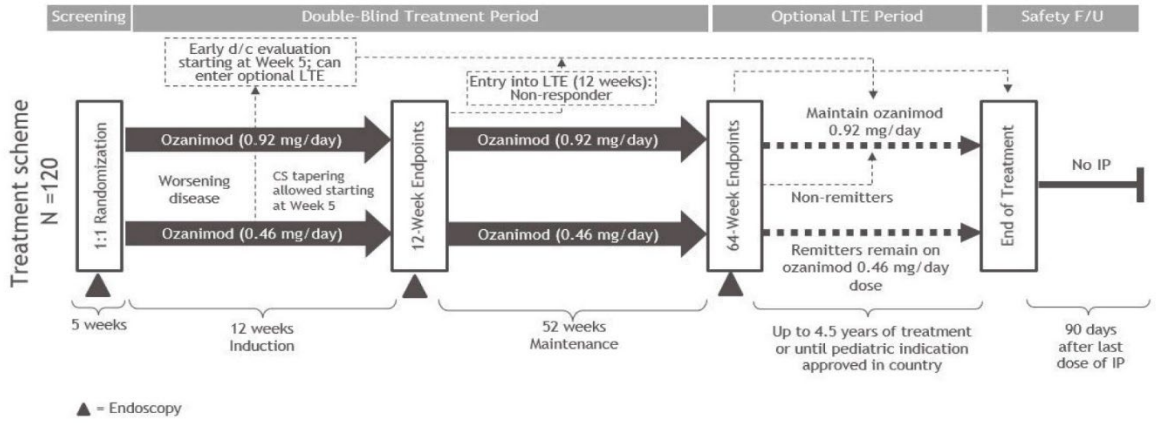
Randomisation and blinding (masking)

Randomization schedules were shipped directly to a pharmacist or other individual(s) who was responsible for the dispensing of blinded study intervention. This (these) individual(s) will be unblinded to study intervention identification but will not be involved in any other aspect of study conduct. The randomization schedules will be maintained in a secure location with access limited to authorized personnel. Blinding of study treatment assignment is critical to the integrity of this clinical study. There is no information that an event of a medical emergency or pregnancy in an individual participant in which knowledge of the IP required unblinding for that participant.

Statistical Methods

The study planned to include a 64-week double-blind treatment period followed by an optional LTE Period of up to approximately 4.5 years. Subjects who met the early discontinuation criteria after at least 7 weeks of treatment in the Induction Period, had confirmed disease worsening during the Maintenance Period, completed Week 12 and were non-responders, or completed Week 64 could enter the LTE Period.

Figure 1: Study Design Schema for Study IM047023



Abbreviations: CS, corticosteroid; d/c, discontinuation; F/U, follow-up; IP, investigational product; LTE, long-term extension period; N, number.

Source: Figure 5.1-1 in Study IM047023 Protocol

Results

Participant flow and Recruitment

A total of 12 subjects were enrolled at 6 investigational sites in Belgium, Hungary, Poland, and United States. Of the enrolled subjects, 5 subjects were randomized and treated in Cohort 1: 3 subjects in 0.46 mg/day group and 2 subjects in 0.92 mg/day group. Seven of the 12 enrolled subjects were screen failures. Due to early termination of the study, Cohort 2 and Cohort 3 were never opened for enrolment.

In the ozanimod 0.46-mg group, 2 subjects completed the induction period, entered the LTE period, and discontinued from the LTE period due to termination of the study. One subject discontinued from the induction period due to early termination of the study.

In the ozanimod 0.92-mg group, 1 subject completed the induction period, entered the LTE period, and discontinued from the LTE period due to AE. The subject discontinued from the induction period due to physician decision for worsening disease activity.

Baseline data

The enrolled population included 5 subjects (3M/2F; 15-16 years old) with body mass index ranging from 15.7 to 23.1 kg/m2. All subjects had nonstricturing, non-penetrating CD. Involved locations included colonic CD, ileocolonic CD, ileal CD. Only one subject had CD history.

Diagnosis and main criteria for inclusion:

Key eligibility criteria included male and female paediatric subjects aged 2 to 17 years, inclusive, who and their parent or guardian signed informed consent form and assent and met the following key target disease criteria:

- Diagnosis of CD ≥ 3 months prior to the Screening Visit, confirmed by clinical and endoscopic evidence and corroborated by a histopathology report.
- PCDAI ≥ 30 and an SES-CD score of ≥ 6 (or SES-CD ≥ 4 in subjects with isolated ileal disease)
- Inadequate response, intolerance, or loss of response to at least 1 of the following treatments for CD: corticosteroids, immunomodulators, biologic therapy, or other systemic immunomodulatory therapies for CD.

Number analysed

After the titration period, which consisted of 4 days of 0.23mg oral followed by 3 days of 0.46mg orally, treatment with the full dose was initiated. The exposure to the full dose ranged from 60 days to 114 days.

Efficacy results

At the time of study termination, none of 5 randomized subjects reached the Week 64 for the primary or secondary endpoints. Only 1 subject in the ozanimod 0.92-mg group reached Week 12 for secondary endpoints. Efficacy results are presented for all visits available.

Clinical Remission by PCDAI:

None of the 5 subjects achieved clinical remission by PCDAI during the study.

Clinical Response by PCDAI:

In the ozanimod 0.46-mg group, 2 subjects achieved clinical response by PCDAI: 1 subject at Week 4, Week 8, LTE Week 4, and LTE end of treatment visit and the other subject at Week 4 and Week 8.

In the ozanimod 0.92-mg group, 1 out of 2 subjects achieved clinical response by PCDAI at Week 8.

Endoscopic Remission by SES-CD:

In the ozanimod 0.46-mg group, post-baseline SES-CD data were not available for any of the 3 subjects.

The one subject in the ozanimod 0.92-mg group who had post baseline SES-CD data at Week 12 and LTE Day 1 did not achieve endoscopic remission.

Endoscopic Response by SES-CD:

The one subject in the ozanimod 0.92-mg group who had post baseline SES-CD data at Week 12 and LTE Day 1 did not achieve endoscopic response.

Symptomatic Remission:

None of the 5 subjects achieved symptomatic remission during the study.

Change from Baseline in Stool Frequency Score and Abdominal Pain Over Time:

Overall, across the 5 subjects, there was no definitive trend observed in the change from baseline in stool frequency score and abdominal pain over time.

Clinical Remission by CDAI:

In the ozanimod 0.46-mg group, none of the 3 subjects achieved clinical remission by CDAI during the study.

In the ozanimod 0.92-mg group, 1 out of 2 subjects achieved clinical remission by CDAI at Week 8.

Clinical Response by CDAI:

In the ozanimod 0.46-mg group, 1 subject achieved clinical response by CDAI at Week 4 and Week 8. The clinical response by CDAI was not evaluable in the other 2 subjects as baseline CDAI values were not available.

In the ozanimod 0.92-mg group, 1 subject achieved clinical response by CDAI at Week 8. The clinical response by CDAI was not evaluable in the other subject as baseline CDAI value was not available.

Overall, across the 5 subjects, there was no definitive trend observed in the change from baseline in stool frequency score and abdominal pain over time.

Safety results

Table 1: Summary of Subjects with Adverse Events - Treated Subjects

	Ozanimod 0.46 mg N=3	**Ozanimod 0.92 mg N=2**
Deaths	0	0
Serious TEAEs	0	1
Related serious TEAEs	0	0
Discontinued due to TEAEs	0	1
TEAEs	2	2
Related TEAEs	0	0
AESIs	-	-
Clostridium difficile infection	0	1

MedDRA: 27.1

TEAEs

Of the 5 treated subjects, 4 subjects experienced at least 1 TEAE: 2 subjects in the ozanimod 0.46-mg group and 2 subjects in the ozanimod 0.92-mg group. TEAEs reported in more than 1 subject included Crohn's disease and COVID-19.

Two subjects in the ozanimod 0.92mg group reported severe TEAEs: Crohn's disease in 1 subject and Crohn's disease, Clostridium difficile infection, and ulcerative colitis in the other subject. The rest of the TEAEs were mild or moderate in intensity. None of TEAEs reported in the study were considered related to study treatment by the investigator.

Serious TEAEs

One subject in the ozanimod 0.92-mg group reported serious TEAEs of Crohn's disease, Clostridium difficile infection, and ulcerative colitis; all events were severe, but were not considered related to study treatment, and resolved.

Deaths

There were no deaths reported in this study.

TEAEs Leading to Treatment Discontinuation

One subject in the ozanimod 0.92-mg group reported a severe TEAE of Crohn's disease that led to discontinuation of the study treatment. The subject's duration of treatment was 114 days.

Adverse Events of Clinical Interest

One subject in the ozanimod 0.92-mg group reported an AESI of Clostridium difficile infection. The event was severe in intensity, serious, and not related to the study treatment. The event outcome was reported as resolved.

Laboratory Assessments, Vital Signs, ECGs

There were no clinically significant abnormalities observed in the haematology and blood chemistry parameters across the 5 subjects. There were no subjects with elevations of ALT or AST ≥ 3 × ULN.

There were no clinically relevant changes from baseline in vital signs measurements for the 5 subjects.

Overview of pharmacodynamics

PD results for ALC and faecal calprotectin were provided. Due to the small sample size, no meaningful interpretation of the results could be made.

2.3.3. Discussion on clinical aspects

The MAH has presented a final clinical study report with data from 5 patients of the 12 patients screened in an expected enrolment of 120 patients in the trial.

Two patients attended up to visit of D1 followed by LTE and follow ups at days 30 and 90. One patient attended up to visit of Week 8, had a SAE (Cl difficile infection, worsening of colitis) had LTE and follow ups at days 30 and 90. One patient attended up to visit of D1 followed by LTE and follow ups at days 30 and 90. One patient has attended up to visit Week8 and had the end of treatment visit later and did not had follow up visits nor it was stated that the patient was lost to follow up nor that the consent was withdrawn. This is a protocol deviation which has not been discussed and was raised as a concern to be responded by the MAH. The MAH justified that the parent / guardian of the child withdrew their consent at the end of treatment visit, thus no further contact was kept.

Regarding efficacy, most patients were not exposed to treatment for a sufficient duration to expect symptomatic nor endoscopic remission, although one patient in the higher 0.92 mg dose entered into clinical remission (not symptomatic).

As for safety, four patients had TEAEs, and patient who was on the 0.92 mg had a serious adverse event and discontinued study treatment.

There were no deaths during the study. Besides description of AEs, there were no serious AEs related to clinical observation nor to laboratory results.

3. Rapporteur's overall conclusion and recommendation

The MAH has presented a final study report of study IM047023 that was prematurely stopped due to Sponsor decision described as not safety related. Notwithstanding, the reason for discontinuation was not provided until the specific request from CHMP. The MAH has justified the cessation of the study due to the lack of positive results in the adult study on Crohn's disease. This is adequate.

☒ **Fulfilled: No regulatory action required.**

4. Request for supplementary information

Based on the data submitted, the MAH should address the following questions as part of this procedure:

1) The MAH has declared that the sponsor decided to stop the study for the reason presented in the *Dear Investigator Letter*. However, this letter could not be found in the documentation accompanying the procedure, and CHMP would like to understand the reason for stopping the paediatric study.

2) As explicit in the protocol, unless the patient withdraws the consent or was lost to follow-up, a follow-up period with 30- and 90-day assessment was expected: With the exception of participants who withdraw consent/assent or are lost to follow-up, participants who discontinue the study should complete the 30-day (± 14 days) and 90-day (± 10 days) Safety Follow-up Visit after the last dose for the collection of safety data and to assess their disease status. Alternative treatment for CD can be started, if needed, after the ET Visit. One patient did not have the safety follow up performed, and there was no discussion on this. The MAH is invited to discuss this finding.

The timetable is a 30-day response timetable with clock stop.

5. MAH responses to Request for supplementary information

Question 1

The MAH has declared that the sponsor decided to stop the study for the reason presented in the Dear Investigator Letter. However, this letter could not be found in the documentation accompanying the procedure, and CHMP would like to understand the reason for stopping the paediatric study.

Summary of the MAH's response

BMS (MAH) announced on 28 March 2024 that Induction Study #2 in adults (RPC01-3202) from the Phase 3 adult Crohn's disease program did not meet its primary endpoint. The development of ozanimod as treatment for paediatric Crohn's Disease was based on the hypothesis that a positive benefit-risk profile of ozanimod in adult Crohn's disease would translate into a similar effect in paediatric CD, the negative outcome of the 3202 study invalidated this hypothesis. BMS has therefore made the difficult decision to terminate the entire ozanimod Phase 3 Crohn's disease program including the ongoing paediatric study, IM047-023. The MAH would like to emphasize that the termination of these studies is in no way related to any new safety signals associated with the use of ozanimod [BMS 986374], nor ozanimod efficacy in patients with ulcerative colitis or multiple sclerosis. The Dear Investigator Letter is provided for assessment

Assessment of the MAH's response

The MAH has duly responded to the request and has provided an adequate justification for the cessation of the paediatric study, which is related to the failure of the equivalent adult study to achieve its objective. The MAH has thus guessed that the paediatric study would likely not achieve its goal either. Even in the unlikely possibility that the paediatric study would result positive, it would still be arguable that it would go against the results from the adult study, and that the positive paediatric study might have been a fortuitous result. It is understood the MAH position.

Conclusion: Issue considered resolved.

Question 2

As explicit in the protocol, unless the patient withdraws the consent or was lost to follow-up, a follow-up period with 30- and 90-day assessment was expected: With the exception of participants who withdraw consent/assent or are lost to follow-up, participants who discontinue the study should complete the 30-day (± 14 days) and 90-day (± 10 days) Safety Follow-up Visit after the last dose for the collection of safety data and to assess their disease status. Alternative treatment for CD can be started, if needed, after the ET Visit. One patient did not have the safety follow up performed, and there was no discussion on this. The MAH is invited to discuss this finding.

Summary of the MAH's response

The MAH acknowledges the protocol requirement that all patients participating in this CD paediatric study (IM047-023) complete the 30-day (± 14 days) and 90-day (± 10 days) Safety Follow-up visits after the study treatment last dose, for the collection of safety data and assessment of disease status. The exception to this requirement is if the patient is lost to follow-up or if consent/assent is withdrawn for this study, which is the case for this subject.

Subject started their first dose of study treatment. The parent/guardian of this patient withdrew consent during the End of Treatment (EoT) visit three months later (); vital signs were assessed but consent was withdrawn for all other EoT study procedures. In addition, no safety follow-up visits or procedures could be performed, as documented in Electronic Data Capture (EDC). While in the study, this patient did not have a treatment-emergent adverse events (TEAE). Protocol deviations were recorded for the EoT procedures that this patient missed due to withdrawal of consent during the EoT visit.

Assessment of the MAH's response

The MAH has now justified the lack of safety follow-up visits due to the withdrawal of consent from the parent / guardian of the concerned subject to continue participation in the study at the end of treatment visit. This had not been presented in the original submission, hence the request for this clarification. It is understood that if the consent is withdrawn and the parent / guardian do not intend to finalize the study, they have this right, and the MAH cannot obtain this safety data in any other way

Conclusion: Issue considered solved.