Clinical trial results:
A Prospective, Multicenter, Single-arm, Open-label, Interventional Phase IV Study to Evaluate the Safety and Efficacy of Idursulfase (r-DNA origin) (Elaprase™) in Indian Pediatric and Adult Population with Hunter Syndrome (Mucopolysaccharidosis II)

Summary

EudraCT number	2022-004193-39
Trial protocol	Outside EU/EEA
Global end of trial date	18 April 2024

Results information

Result version number	v1 (current)
This version publication date	03 January 2025
First version publication date	03 January 2025

Trial information

Trial identification

Sponsor protocol code	TAK-665-4001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05058391
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda Biopharmaceuticals India Pvt. Ltd.
Sponsor organisation address	Building No. 8, 6th Floor, Tower C, DLF Cyber City, Gurgaon, Haryana, India, 122002
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the safety and efficacy of elaprase in Indian pediatric and adult participants with Hunter Syndrome.

Protection of trial subjects:

Each participant or their parents/guardians/legally authorized representatives signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 April 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	India: 5
Worldwide total number of subjects	5
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	4
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at investigative sites in India from 21 April 2022 to 18 April 2024.

Pre-assignment

Screening details:

Participants with a diagnosis of Hunters Syndrome were enrolled in this study to receive elaprase intravenous (IV) infusion.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Elaprase 0.5 mg/kg

Arm description:

Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

Arm type	Experimental
Investigational medicinal product name	Elaprase
Investigational medicinal product code	
Other name	Idursulfase
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

Number of subjects in period 1	Elaprase 0.5 mg/kg
Started	5
Completed	4
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Elaprase 0.5 mg/kg
Reporting group description:	
Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.	

Reporting group values	Elaprase 0.5 mg/kg	Total	
Number of subjects	5	5	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	8.0		
standard deviation	± 4.85	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	5	5	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	5	5	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	5	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Elaprase 0.5 mg/kg

Reporting group description:

Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

Subject analysis set title	Elaprase 0.5 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single dose of elaprase 0.5 milligrams per kilogram (mg/kg) intravenous infusion every week on Day 1 up to end of treatment (EOT) (Day 358, Week 52).

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuation due to TEAEs and Death

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuation due to TEAEs and Death[1]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (example, a clinically significant abnormal laboratory value), symptom, or disease temporally associated with the use of a drug whether or not it is considered related to the drug. A serious TEAE was defined as any untoward medical occurrence that at any dose results in: death; is life-threatening: requires inpatient hospitalization or results in prolongation of existing hospitalization; persistent or significant disability/incapacity; leads to a congenital anomaly/birth defect or is an important medical event. Number of participants with TEAEs, serious TEAEs, discontinuation due to TEAEs, and death are reported. The SAS included all participants who received at least one dose of study drug at any time during trial.

End point type	Primary

End point timeframe:

From start of the study drug administration up to Week 53

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned for this endpoint.

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: participants				
TEAEs	5			
Serious TEAEs	1			
Discontinuation due to TEAEs	1			
Death	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Drug Reactions (ADRs)

End point title	Number of Participants With Adverse Drug Reactions (ADRs)[2]

End point description:

An ADR was defined as a response to a drug which was noxious and unintended, and which occurred at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. The SAS included all participants who received at least one dose of study drug at any time during trial.

End point type	Primary

End point timeframe:

From start of the study drug administration up to Week 53

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned for this endpoint.

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Infusion-related Reactions (IRRs)

End point title	Number of Participants With Infusion-related Reactions

End point description:

An IRR was defined as an AE that had been assessed as at least possibly related to treatment with elaprase and occurred during an infusion or up to 24 hours post-infusion. The SAS included all participants who received at least one dose of study drug at any time during trial.

End point type	Primary

End point timeframe:

From start of the study drug administration up to Week 53

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned for this endpoint.

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percentage Forced Vital Capacity (%FVC) at

Weeks 27 and 53

End point title	Change From Baseline in Percentage Forced Vital Capacity (%FVC) at Weeks 27 and 53

End point description:

FVC is the amount of air that can be forcibly exhaled from your lungs after taking the deepest breath possible, as measured by spirometry. FVC is a measure of respiratory function. The Full Analysis Set (FAS) included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: %FVC				
arithmetic mean (standard deviation)				
Week 27	-2.0 (± 4.24)			
Week 53	1.0 (± 2.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 6 Minute Walk Test (6MWT) at Weeks 27 and 53

End point title	Change From Baseline in 6 Minute Walk Test (6MWT) at Weeks 27 and 53

End point description:

6MWT is the distance covered over a time of 6 minutes and is a measure of physical functional capacity which is determined on a walking course. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: meters				
arithmetic mean (standard deviation)				
Week 27	24.3 (± 24.31)			

Week 53	184.8 (± 138.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cardiac Left Ventricular Mass Index (LVMI) at Weeks 27 and 53

End point title	Change From Baseline in Cardiac Left Ventricular Mass Index (LVMI) at Weeks 27 and 53

End point description:

Cardiac LVMI was measured by 2-dimensional (2D) echocardiography. Cardiac LVMI is the left ventricular mass (LVM) in grams indexed to body surface area (BSA), in square meters (m^2). Cardiac LVMI (in grams per square meter [g/m^2])=LVM divided by BSA. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: g/m^2				
arithmetic mean (standard deviation)				
Week 27	-12.0 (± 20.91)			
Week 53	-20.9 (± 15.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) at Weeks 27 and 53

End point title	Change From Baseline in Left Ventricular Ejection Fraction (LVEF) at Weeks 27 and 53

End point description:

The LVEF was measured by 2D echocardiography and considered a sufficiently sensitive measure to evaluate any changes in cardiac function. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: percentage of LVEF				
arithmetic mean (standard deviation)				
Week 27	4.1 (± 3.30)			
Week 53	6.6 (± 7.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Liver Volume at Weeks 27 and 53

End point title	Change From Baseline in Liver Volume at Weeks 27 and 53

End point description:

Liver volume was determined by Ultrasonography (USG). The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: cubic centimeters (cm^3)				
arithmetic mean (standard deviation)				
Week 27	67.0 (± 245.27)			
Week 53	175.3 (± 255.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Spleen Volume at Weeks 27 and 53

End point title	Change From Baseline in Spleen Volume at Weeks 27 and 53

End point description:

Spleen volume was determined by USG. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: cm^3				
arithmetic mean (standard deviation)				
Week 27	48.3 (± 129.60)			
Week 53	123.7 (± 207.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Normalized Urine Glycosaminoglycan (uGAG) Levels at Week 14, 27, 40, and 53

End point title	Change From Baseline in Normalized Urine Glycosaminoglycan (uGAG) Levels at Week 14, 27, 40, and 53

End point description:

Normalized uGAG was analyzed using urine testing. The uGAG levels were normalized to urine creatinine and were reported as microgram glycosaminoglycan (GAG) per milligram creatinine (µg GAG/mg creatinine). The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. 'n' indicates the number of participants with data available for analysis for the specified category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 14, 27, 40, and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: µg GAG/mg creatinine				
arithmetic mean (standard deviation)				
Week 14 (n=5)	33.3 (± 112.91)			
Week 27 (n=4)	-28.9 (± 31.92)			

Week 40 (n=4) Week 53 (n=4)	123.4 (± 222.41) 8.6 (± 29.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Global Joint Range of Motion (JROM) Score at Weeks 27 and 53

End point title	Change From Baseline in Global Joint Range of Motion (JROM) Score at Weeks 27 and 53

End point description:

Passive joint mobility:Range of motion of shoulder,elbow,wrist,hip,knee &ankle joints, as assessed by 1 expert physician using universal goniometry method. Global JROM (% of normal range of motion) is average of 11 ratiosX100. Ratios are left/right means of passive range of motion in shoulder(flexion/extension, abduction, internal/external rotation), elbow (flexion/extension), wrist (flexion/extension), index finger (flexion/extension [combined metacarpophalangeal joint, proximal interphalangeal joint, distal interphalangeal joint motion]), hip (flexion/extension, abduction, internal/external rotation), knee (flexion/extension) & ankle (dorsiflexion) divided by normal range (American Academy of Orthopedic Surgeons and American Medical Association). FAS included all enrolled participants who received at least 1 dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: percentage of normal range of motion				
arithmetic mean (standard deviation)				
Week 27 Week 53	-8.0 (± 7.14) -14.0 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Anthropometric Parameter: Height at Weeks 27 and 53

End point title	Change From Baseline in Anthropometric Parameter: Height at Weeks 27 and 53

End point description:

Change from baseline in height (centimeters [cm]) was assessed in participants less than (<)18 years of

age. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: cm				
arithmetic mean (standard deviation)				
Week 27	3.0 (± 2.34)			
Week 53	3.7 (± 3.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Anthropometric Parameter: Weight at Weeks 27 and 53

End point title	Change From Baseline in Anthropometric Parameter: Weight at Weeks 27 and 53

End point description:

Change from baseline in weight (kilograms[kg]) was assessed in all participants. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: kg				
arithmetic mean (standard deviation)				
Week 27	0.3 (± 1.50)			
Week 53	1.6 (± 1.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health-related Quality of Life (HRQoL) Based on Change From Baseline in the Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale (HS-FOCUS) Domain Scores

End point title	Health-related Quality of Life (HRQoL) Based on Change From Baseline in the Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale (HS-FOCUS) Domain Scores

End point description:

HS-FOCUS is developed as disease-specific measure of impact of Hunter syndrome on HRQL. HS-FOCUS is designed to gather information on participant's daily life & wellbeing, satisfaction with treatment & hospitalisations & on how Hunter syndrome impacts participant's general quality of life. HS-FOCUS includes 2 validated components:parent version & participant self-reported version for those over age 12 years. HS-FOCUS (shortened version) questionnaire has 5 function domains (walking/standing, grip/reach, school/work, activities & breathing). Items are scored using response scale from 0-3, with 0=ability to complete activity-related functions 'without any difficulty' & 3=highest disability. Higher scores on each domain indicate greater disability. FAS included all enrolled participants who received at least one dose of study drug & with at least 1 post-baseline evaluation of any of efficacy endpoints. Subjects analysed is number of participants with data available.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)				
Walking/ Standing: Week 27 (n=4)	-0.3 (± 0.22)			
Walking/ Standing: Week 53 (n=4)	-0.5 (± 0.41)			
Grip/Reach: Week 27 (n=4)	-0.1 (± 0.49)			
Grip/Reach: Week 53 (n=4)	-0.1 (± 0.52)			
School/ Work: Week 27 (n=3)	0.3 (± 0.58)			
School/ Work: Week 53 (n=3)	-1.0 (± 1.73)			
Activities: Week 27 (n=4)	-0.1 (± 0.25)			
Activities: Week 53 (n=4)	-0.9 (± 1.03)			
Breathing: Week 27 (n=4)	-0.7 (± 0.80)			
Breathing: Week 53 (n=4)	-0.8 (± 1.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the HRQoL Based on Childhood Health Assessment Questionnaire (CHAQ) Domain Scores

End point title	Change From Baseline in the HRQoL Based on Childhood Health Assessment Questionnaire (CHAQ) Domain Scores

End point description:

The CHAQ was initially developed for assessing juvenile idiopathic arthritis, from the perspective of the

parent or participant, and has been previously applied to other chronic disabling conditions such as Hunter syndrome. It is a 30-item instrument that measures functional capacity and independence in activities of daily life across eight domains: dressing and grooming, arising, eating, walking, reach, grip, hygiene, and activities. For each domain, there is a 4-level difficulty scale that is scored from 0 to 3, with 0 corresponding to 'without any difficulty' and 3 to 'unable to do'. Higher scores on each domain indicate greater disability. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Weeks 27 and 53

End point values	Elaprase 0.5 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)				
Dressing/ Grooming: Week 27	0.0 (± 2.16)			
Dressing/ Grooming: Week 53	-0.5 (± 2.65)			
Arising: Week 27	-0.3 (± 0.50)			
Arising: Week 53	-0.3 (± 0.50)			
Eating: Week 27	-0.3 (± 0.50)			
Eating: Week 53	-0.3 (± 0.50)			
Walking: Week 27	-0.3 (± 0.50)			
Walking: Week 53	-0.3 (± 0.50)			
Hygiene: Week 27	-0.5 (± 0.58)			
Hygiene: Week 53	-0.8 (± 0.96)			
Reach: Week 27	-1.0 (± 1.41)			
Reach: Week 53	-0.8 (± 0.96)			
Grip: Week 27	-0.5 (± 1.00)			
Grip: Week 53	-1.3 (± 1.50)			
Activities: Week 27	0.0 (± 0.00)			
Activities: Week 53	-0.5 (± 1.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study drug administration up to Week 53	
Adverse event reporting additional description:	
The SAS included all participants who received at least one dose of study drug at any time during trial.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Elaprase 0.5 mg/kg
Reporting group description:	
Participants received a single dose of elaprase 0.5 milligrams per kilogram (mg/kg) IV infusion every week from Week 1 (Day 1) up to end of treatment (EOT) at Week 52.	

Serious adverse events	Elaprase 0.5 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Elaprase 0.5 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Injury, poisoning and procedural complications			
Limb Injury			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
General disorders and administration site conditions			

Hernia Pain subjects affected / exposed occurrences (all) Infusion Site Extravasation subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Swelling subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1 1 / 5 (20.00%) 3 3 / 5 (60.00%) 7 1 / 5 (20.00%) 1		
Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Gastrointestinal disorders Abdominal Pain Upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Mouth Ulceration subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all)	4 / 5 (80.00%) 6 1 / 5 (20.00%) 1		

Sneezing subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Skin and subcutaneous tissue disorders Dermatitis Allergic subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 4		
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all) Ear Infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 4 / 5 (80.00%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2021	The following changes were made as per amendment 2.0: 1. Updated study inclusion, exclusion and discontinuation criteria.
27 October 2022	The following changes were made as per amendment 3.0 1. Changed the sponsor's name from "Shire Biotech India Pvt. Ltd." to "Takeda Biopharmaceuticals India Pvt. Ltd." and updated all the relevant contact

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported