Clinical trial results:
A Follow-up of a Phase 3 Study to Evaluate the Long-term Safety and Efficacy of Darvadstrocel in the Treatment of Complex Perianal Fistula in Subjects With Crohn's Disease Who Have Participated in ADMIRE II Study

Summary

EudraCT number	2019-000333-39
Trial protocol	CZ FR HU ES BE PL IT
Global end of trial date	02 April 2024

Results information

Result version number	v1 (current)
This version publication date	18 April 2025
First version publication date	18 April 2025

Trial information

Trial identification

Sponsor protocol code	Darvadstrocel-3003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04075825
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Ave, Lexington, Massachusetts, United States, 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Takeda, Study Director, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trials was to evaluate the long-term safety of a single dose of darvadstrocel in participants with crohn's disease (CD) and complex perianal fistula by evaluation of adverse events (AEs), serious adverse events (SAEs), and adverse events of special interest (AESIs).

Protection of trial subjects:

Each participant signed an informed consent form (ICF) before participating in the study.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	05 November 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Israel: 17
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	United States: 55
Worldwide total number of subjects	150
EEA total number of subjects	78

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	147
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 05 November 2019 to 02 April 2024.

Pre-assignment

Screening details:

Participants diagnosed with Complex Perianal Fistula in Crohn's Disease (CD) who completed the Week 52 visit in the parent study ADMIRE-CD II (Cx601-0303, NCT03279081) were enrolled. Participants remained in the treatment group (placebo or darvadstrocel) to which they were assigned in ADMIRE-CD II study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants who received darvadstrocel placebo-matching eASCs intralesional injection previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intralesional use

Dosage and administration details:

Participants who received darvadstrocel placebo-matching eASCs intralesional injection previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Arm title	Darvadstrocel

Arm description:

Participants who received a single dose of darvadstrocel, 120 million cells, intralesionally previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Arm type	Experimental
Investigational medicinal product name	Darvadstrocel
Investigational medicinal product code	Cx601
Other name	Expanded human allogenic mesenchymal adult stem cells extracted from adipose tissue (eASCs)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralesional use

Dosage and administration details:

Participants who received a single dose of darvadstrocel, 120 million cells, intralesionally previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Number of subjects in period 1	Placebo	Darvadstrocel
Started	74	76
Completed	57	63
Not completed	17	13
Consent withdrawn by subject	6	8
Physician decision	3	1
Participation in New Clinical Trial	1	1
Reason Not Specified	2	2
Lost to follow-up	5	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants who received darvadstrocel placebo-matching eASCs intralesional injection previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.	
Reporting group title	Darvadstrocel
Reporting group description:	
Participants who received a single dose of darvadstrocel, 120 million cells, intralesionally previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.	

Reporting group values	Placebo	Darvadstrocel	Total
Number of subjects	74	76	150
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38.9	40.6	
standard deviation	± 11.33	± 12.04	-
Gender categorical Units: Subjects			
Female	28	35	63
Male	46	41	87
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	73	68	141
More than one race	0	0	0
Unknown or Not Reported	1	7	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	4	9
Not Hispanic or Latino	65	62	127
Unknown or Not Reported	4	10	14

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants who received darvadstrocel placebo-matching eASCs intralesional injection previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Reporting group title	Darvadstrocel

Reporting group description:

Participants who received a single dose of darvadstrocel, 120 million cells, intralesionally previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs)[1]

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered an investigational medicinal product; 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 finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. A TEAE is defined as any event emerging or manifesting at or after the initiation of treatment with a study intervention or medicinal product or any existing event that worsens in either intensity or frequency following exposure to the study intervention or medicinal product.

End point type	Primary

End point timeframe:

Baseline (Week 0) up to Week 104 of this study (Week 52 up to Week 156 in relation to ADMIRE-CD II)

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 analyses was planned for this endpoint.

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: participants	40	43		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment Emergent Serious Adverse Events (TESAEs)[2]

End point description:

TEAE is defined as: any adverse event emerging/manifesting at or after the initiation of treatment with a study intervention/medicinal product or any existing event that worsens in either intensity/frequency following exposure to the study intervention/medicinal product. Serious adverse event (SAE) is an untoward medical occurrence, significant hazard, contraindication, side effect/precaution that at any

dose: results in death, is life-threatening, required in-patient hospitalization/prolongation of existing hospitalization, results in persistent/significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant.

End point type	Primary

End point timeframe:

Baseline (Week 0) up to Week 104 of this study (Week 52 up to Week 156 in relation to ADMIRE-CD II)

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 analyses was planned for this endpoint.

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: participants	14	11		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Specific Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Specific Adverse Events of Special Interest (AESIs)[3]

End point description:

AESIs are AEs that are not solicited local or systemic AEs, they are predefined AEs that require close monitoring and prompt reporting to the sponsor. Protocol pre-specified AESIs included immunogenicity/allo-immunoreactions, tumorigenicity, ectopic tissue formation and fistula/abscess. In addition, ad hoc AESIs of anaphylactic reaction, hypersensitivity, and malignancy.

End point type	Primary

End point timeframe:

Baseline (Week 0) up to Week 104 of this study (Week 52 up to Week 156 in relation to ADMIRE-CD II)

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 analyses was planned for this endpoint.

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: participants				
Immunogenicity/Allo-immunoreactions	3	7		
Tumorgenicity	1	3		
Fistula, Abscess	6	7		
Ectopic Tissue Formation	1	0		
Hypersensitivity	3	3		
Anaphylactic Reaction	0	0		
Malignancy	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieve Clinical Remission at Weeks 104 and 156 (After IMP Administration in ADMIRE-CD II Study)

End point title	Percentage of Participants who Achieve Clinical Remission at Weeks 104 and 156 (After IMP Administration in ADMIRE-CD II Study)

End point description:

Clinical remission is defined as closure of all treated external fistula openings that were draining at baseline of ADMIRE-CD II despite gentle finger compression. Percentages were rounded off to the nearest second decimal place.

End point type	Secondary

End point timeframe:

At Weeks 52 and 104 of this study (Weeks 104 and 156 in relation to ADMIRE-CD II, respectively)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: percentage of participants				
number (confidence interval 95%)				
Week 52	36.49 (25.52 to 47.45)	50.00 (38.76 to 61.24)		
Week 104	31.08 (20.54 to 41.63)	43.42 (32.28 to 54.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieve Clinical Response at Weeks 104 and 156 (After IMP Administration in ADMIRE-CD II Study)

End point title	Percentage of Participants who Achieve Clinical Response at Weeks 104 and 156 (After IMP Administration in ADMIRE-CD II Study)

End point description:

Clinical response is defined as closure of at least 50% of all treated external fistula openings that were draining at baseline of ADMIRE-CD II despite gentle finger compression. Percentages were rounded off to the nearest second decimal place.

End point type	Secondary

End point timeframe:

At Weeks 52 and 104 of this study (Weeks 104 and 156 in relation to ADMIRE-CD II, respectively)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: percentage of participants				
number (confidence interval 95%)				
Week 52	40.54 (29.35 to 51.73)	56.58 (45.44 to 67.72)		
Week 104	32.43 (21.77 to 43.10)	47.37 (36.14 to 58.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieve Combined Remission at Week 156 (After IMP Administration in ADMIRE-CD II Study)

End point title	Percentage of Participants who Achieve Combined Remission at Week 156 (After IMP Administration in ADMIRE-CD II Study)

End point description:

Combined remission of complex perianal fistula(s) is defined as the clinical assessment of closure of all treated external openings that were draining at baseline of ADMIRE-CD II, despite gentle finger compression, and absence of collection(s) >2 cm (in at least 2 dimensions) of the treated perianal fistula(s) confirmed by centrally read blinded MRI assessment. Percentages were rounded off to the nearest second decimal place.

End point type	Secondary

End point timeframe:

At Week 104 of this study (Week 156 in relation to ADMIRE-CD II)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: percentage of participants				
number (confidence interval 95%)	29.73 (19.32 to 40.14)	36.84 (26.00 to 47.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With New Anal Abscess in Treated Fistula at Week 156

End point title	Percentage of Participants With New Anal Abscess in Treated Fistula at Week 156

End point description:

Percentages were rounded off to the nearest second decimal place.

End point type	Secondary

End point timeframe:

At Week 104 of this study (Week 156 in relation to ADMIRE-CD II)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	76		
Units: percentage of participants				
number (confidence interval 95%)	9.62 (3.20 to 21.03)	7.02 (1.95 to 17.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Relapse at Week 156 After Achieving Combined Remission at Week 52 of ADMIRE-CD II

End point title	Percentage of Participants With Relapse at Week 156 After Achieving Combined Remission at Week 52 of ADMIRE-CD II

End point description:

Relapse is defined as participants who were in combined remission at Week 52 of ADMIRE-CD II and who have either reopening of any of the treated fistula(s) external openings with active drainage as clinically assessed or, the development of a perianal fluid collection >2 cm of the treated perianal fistulas confirmed by centrally read magnetic resonance imaging (MRI) assessment. Combined remission at Week 52 was defined as clinically assessed closure of all treated external openings that were draining at baseline of ADMIRE-CD II, despite gentle finger compression, and absence of collection(s) >2 cm (in at least 2 dimensions) of the treated perianal fistula(s) confirmed by blinded central MRI assessment. Percentages were rounded off to the nearest second decimal place.

End point type	Secondary

End point timeframe:

At Week 104 of this study (Week 156 in relation to ADMIRE-CD II)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	40		
Units: percentage of participants				
number (confidence interval 95%)	54.76 (39.71 to 69.81)	42.50 (27.18 to 57.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of ADMIRE-CD II in Scores of Discharge Items of Perianal Disease Activity Index (PDAI) Score at Weeks 104 and 156

End point title	Change from Baseline of ADMIRE-CD II in Scores of Discharge Items of Perianal Disease Activity Index (PDAI) Score at Weeks 104 and 156

End point description:

The PDAI is a scoring system to evaluate the severity of perianal CD. From the 5-item instrument, only 'discharge' was used for this outcome measure. Each category is graded on a 5-point Likert scale ranging from no symptoms (score of 0) to severe symptoms (score of 4); a higher score indicates more severe disease.

End point type	Secondary

End point timeframe:

From Baseline of ADMIRE-CD II up to Weeks 52 and 104 of this study (From Baseline up to Weeks 104 and 156 in relation to ADMIRE-CD II, respectively)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	67		
Units: score on a scale				
arithmetic mean (standard deviation)				
ADMIRE-CD II Baseline (BL) Score	1.53 (± 1.072)	1.25 (± 0.893)		
Change from ADMIRE-CD II BL to Week52(this study)	-0.67 (± 1.178)	-0.56 (± 1.218)		
Change from ADMIRE-CD II BL to Week104(this study)	-0.67 (± 1.279)	-0.50 (± 1.128)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of ADMIRE-CD II in Scores of Pain Items of Perianal Disease Activity Index (PDAI) Score at Weeks 104 and 156

End point title	Change from Baseline of ADMIRE-CD II in Scores of Pain Items of Perianal Disease Activity Index (PDAI) Score at Weeks 104 and 156

End point description:

The PDAI is a scoring system to evaluate the severity of perianal CD. From the 5-item instrument, only 'pain' was used for this outcome measure. Each category is graded on a 5-point Likert scale ranging from no symptoms (score of 0) to severe symptoms (score of 4); a higher score indicates more severe disease.

End point type	Secondary

End point timeframe:

From Baseline of ADMIRE-CD II up to Weeks 52 and 104 of this study (From Baseline up to Weeks 104 and 156 in relation to ADMIRE-CD II, respectively)

End point values	Placebo	Darvadstrocel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	67		
Units: score on a scale				
arithmetic mean (standard deviation)				
ADMIRE-CD II Baseline (BL) Score	1.25 (± 1.060)	1.06 (± 0.936)		
Change from ADMIRE-CD II BL to Week52(this study)	-0.49 (± 1.391)	-0.54 (± 1.010)		
Change from ADMIRE-CD II BL to Week104(this study)	-0.56 (± 1.271)	-0.45 (± 1.060)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 104 weeks in this study (From Week 52 to Week 156 in relation to ADMIRE-CD II)

Adverse event reporting additional description:

Safety Analysis Set included all participants enrolled in the LTE study, according to the actual treatment they received in the ADMIRE-CD II study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Darvadstrocel

Reporting group description:

Participants who received a single dose of darvadstrocel, 120 million cells, intralesionally previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Reporting group title	Placebo

Reporting group description:

Participants who received darvadstrocel placebo-matching eASCs intralesional injection previously in the ADMIRE-CD II study were observed for efficacy and safety. No drug was administered in this study.

Serious adverse events	Darvadstrocel	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 76 (14.47%)	14 / 74 (18.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Gastrointestinal stoma complication			

subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anorectal disorder			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 76 (1.32%)	2 / 74 (2.70%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	1 / 76 (1.32%)	2 / 74 (2.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	1 / 76 (1.32%)	2 / 74 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Terminal ileitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 76 (1.32%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fistula discharge			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			

subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	3 / 76 (3.95%)	2 / 74 (2.70%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 76 (2.63%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Darvadstrocel	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 76 (18.42%)	11 / 74 (14.86%)	
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	5 / 76 (6.58%)	3 / 74 (4.05%)	
occurrences (all)	5	3	
Infections and infestations			

COVID-19 subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 11	8 / 74 (10.81%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2022	The following change was made as per Amendment 01: The legal entity was changed from Millennium Pharmaceuticals, Inc, to Takeda Development Center Americas, Inc.
17 November 2022	The following changes were made as per Amendment 02: 1. Defined the end of the study. 2. Defined the situations in which a participant was considered a treatment failure. 3. Included the option of remote site visits in sites/countries where allowed by local legislation. 4. Included an interim analysis (IA).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported