



## Clinical trial results:

### A Phase 1/2, Open-Label Safety and Dose-Finding Study of Adeno-Associated Virus (AAV) Serotype 8 (AAV8)-Mediated Gene Transfer of Glucose-6-Phosphatase (G6Pase) in Adults with Glycogen Storage Disease Type Ia (GSDIa)

#### Summary

EudraCT number	2016-003023-30
Trial protocol	ES NL
Global end of trial date	02 November 2021

#### Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

#### Trial information

##### Trial identification

Sponsor protocol code	401GSDIA01
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03517085
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Ultragenyx Pharmaceutical Inc.
Sponsor organisation address	60 Leveroni Court, Novato, United States, California 94949
Public contact	Patient Advocacy, Ultragenyx Pharmaceutical, Inc., +1 415 756-8657, Trialrecruitment@ultragenyx.com
Scientific contact	Medical Information, Ultragenyx Pharmaceutical, Inc., +1 888 756-8657, medinfo@ultragenyx.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 November 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 November 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to determine the safety of single doses of DTX401, including the incidence of dose-limiting toxicities (DLTs) at each dose level.

Protection of trial subjects:

The trial was designed, conducted, recorded, and reported in accordance with the principles established by the 18th World Medical Association General Assembly (Helsinki, 1964) and subsequent amendments and clarifications adopted by the General Assemblies. The investigators made every effort to ensure that the study was conducted in full conformance with Helsinki principles, International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, current Food and Drug Administration (FDA) regulations, EU Clinical Trial Directive 2001/20/EC, and local ethical and regulatory requirements. Each investigator was thoroughly familiar with the appropriate administration and potential risks of administration of the study drug, as described in the protocol and Investigator's Brochure, prior to the initiation of the study. The method of obtaining and documenting informed consent and the contents of the informed consent form (ICF) complied with ICH GCP guidelines, the requirements of 21 CFR Part 50, "Protection of Human Subjects," the Health Insurance Portability and Accountability Act regulations, and all other applicable regulatory requirements. Investigators were responsible for preparing the ICF and submitting it to the Sponsor for approval prior to submission to the Institutional Review Board (IRB). All ICFs were written in regional language and contained the minimum elements for consent as mandated by the ICH guidelines. An IRB-approved ICF was provided by the Sponsor prior to initiation of the study. Investigators obtained signed written informed consent from each potential study subject prior to the conduct of any study procedures and after the methods, objectives, requirements, and potential risks of the study were fully explained to each potential subject. Consent for participation could be withdrawn at any time for any reason by the subject.

Background therapy:

During the study, participants were administered oral prednisone or prednisolone as a reactive ( Cohorts 1 and 2; 6 weeks, at a starting dose of 40 mg/day, after ALT elevation), optimized reactive (Cohort 3; 7 weeks, at a starting dose of 60 mg/day, after ALT elevation), or prophylactic (Cohort 4; 8 weeks, at a starting dose of 60 mg/day, starting on Day 1) regimen to manage alanine aminotransferase (ALT) elevation.

Evidence for comparator: -

Actual start date of recruitment	18 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Canada: 1

Worldwide total number of subjects	12
EEA total number of subjects	3

Notes:

<b>Subjects enrolled per age group</b>	
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)	12
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Eligible participants were enrolled sequentially into 4 cohorts of 3 participants each and received a single intravenous (IV) infusion of DTX401, with steroids (prednisone/prednisolone) to manage alanine aminotransferase (ALT) elevation.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	DTX401 Cohort 1

Arm description:

DTX401 Dose 1 ( $2.0 \times 10^{12}$  GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)

Arm type	Experimental
Investigational medicinal product name	DTX401
Investigational medicinal product code	
Other name	AAV8G6PC, Pariglasgene brecaparvovec
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

DTX401 administered as a single peripheral intravenous (IV) infusion

<b>Arm title</b>	DTX401 Cohort 2
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Arm description:

DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)

Arm type	Experimental
Investigational medicinal product name	DTX401
Investigational medicinal product code	
Other name	AAV8G6PC, Pariglasgene brecaparvovec
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

DTX401 administered as a single peripheral intravenous (IV) infusion

<b>Arm title</b>	DTX401 Cohort 3
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Arm description:

DTX 401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with an optimized reactive steroid regimen (7 weeks, at a starting dose of 60 mg/day, after ALT elevation)

Arm type	Experimental
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Investigational medicinal product name	DTX401
Investigational medicinal product code	
Other name	AAV8G6PC, Pariglasgene breca parvovec
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
DTX401 administered as a single peripheral intravenous (IV) infusion	
<b>Arm title</b>	DTX401 Cohort 4

Arm description:

DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with a prophylactic steroid regimen (8 weeks, at a starting dose of 60 mg/day, starting on Day 1)

Arm type	Experimental
Investigational medicinal product name	DTX401
Investigational medicinal product code	
Other name	AAV8G6PC; Pariglasgene breca parvovec
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

DTX401 administered as a single peripheral intravenous (IV) infusion

<b>Number of subjects in period 1</b>	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3
Started	3	3	3
Completed	3	3	3

<b>Number of subjects in period 1</b>	DTX401 Cohort 4
Started	3
Completed	3

## Baseline characteristics

### Reporting groups

Reporting group title	DTX401 Cohort 1
Reporting group description: DTX401 Dose 1 ( $2.0 \times 10^{12}$ GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 2
Reporting group description: DTX401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 3
Reporting group description: DTX 401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with an optimized reactive steroid regimen (7 weeks, at a starting dose of 60 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 4
Reporting group description: DTX401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with a prophylactic steroid regimen (8 weeks, at a starting dose of 60 mg/day, starting on Day 1)	

Reporting group values	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3
Number of subjects	3	3	3
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	45.3	29.7	26.0
standard deviation	$\pm 15.3$	$\pm 10.1$	$\pm 13.9$
Gender categorical Units: Subjects			
Female	1	0	2
Male	2	3	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	3	2	3
Race Units: Subjects			
White	3	3	3
Controlled Fasting Challenge: Time to First Hypoglycemic Event [			
Time (in hours) to first hypoglycemic event (defined as glucose < 54 mg/dL [ $< 3.0$ mmol/L]) during a controlled fasting challenge.			
Units: hours			
arithmetic mean	4.4	4.5	2.3
standard deviation	$\pm 0.9$	$\pm 1.4$	$\pm 1.2$

Reporting group values	DTX401 Cohort 4	Total	
Number of subjects	3	12	

Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	25.0 ± 5.2	-	
Gender categorical Units: Subjects			
Female	1	4	
Male	2	8	
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	3	11	
Race Units: Subjects			
White	3	12	
Controlled Fasting Challenge: Time to First Hypoglycemic Event [			
Time (in hours) to first hypoglycemic event (defined as glucose < 54 mg/dL [ $< 3.0$ mmol/L]) during a controlled fasting challenge.			
Units: hours arithmetic mean standard deviation	2.5 ± 0.9	-	

## End points

### End points reporting groups

Reporting group title	DTX401 Cohort 1
Reporting group description: DTX401 Dose 1 ( $2.0 \times 10^{12}$ GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 2
Reporting group description: DTX401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 3
Reporting group description: DTX 401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with an optimized reactive steroid regimen (7 weeks, at a starting dose of 60 mg/day, after ALT elevation)	
Reporting group title	DTX401 Cohort 4
Reporting group description: DTX401 Dose 2 ( $6.0 \times 10^{12}$ GC/kg) with a prophylactic steroid regimen (8 weeks, at a starting dose of 60 mg/day, starting on Day 1)	

### Primary: Number of Participants With Adverse Events (AEs) Treatment-Emergent AEs (TEAEs) Serious TEAEs, Discontinuations Due to TEAEs, and Dose-Limiting Toxicities (DLTs)

End point title	Number of Participants With Adverse Events (AEs) Treatment-Emergent AEs (TEAEs) Serious TEAEs, Discontinuations Due to TEAEs, and Dose-Limiting Toxicities (DLTs) <sup>[1]</sup>
End point description: An AE is defined as any untoward medical occurrence, regardless of its causal relationship to study product. An SAE is defined as any event that: results in death; is immediately life threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or an important medical event, in the opinion of the investigator. The relationship to study drug was categorized as unrelated, possible, probable or definite. A DLT is defined as any AE/SAE $\geq$ Grade 3 that is considered by the Investigator and/or Sponsor to be related to DTX401, based on the Nation Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0 or later version. Per protocol, SAEs that occurred > 30 days after EOS or Early withdrawal visit, did not need to be reported unless Investigator considered them related to study product.	
End point type	Primary
End point timeframe: AEs Prior to Dosing: From signing the informed consent form (ICF) to first dose of study drug. TEAEs: From first dose of study drug through the End of Study (EOS)/Early Withdrawal visit (up to Week 52) plus 30 days.	
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: Descriptive statistics are presented per protocol.	

End point values	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3	DTX401 Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: participants				
AE started prior to dosing	1	1	2	2
Any TEAE	3	3	3	3



Related TEAE	3	3	3	3
Serious TEAE	2	1	1	0
Serious related TEAE	0	0	0	0
Grade 3 or 4 TEAE	0	0	1	0
Dose-limiting toxicity	0	0	0	0
TEAE leading to study discontinuation	0	0	0	0
TEAE leading to death	0	0	0	0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Time to First Hypoglycemic Event Over Time

End point title	Change From Baseline in Time to First Hypoglycemic Event Over Time
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End point description:

The change from baseline in time (in hours) to first hypoglycemic event (defined as glucose < 54 mg/dL [ $< 3.0$  mmol/L]) during a controlled fasting challenge at 12, 24, and 52 weeks after IV administration of DTX401. A positive change from baseline is favorable.

n=participants with an assessment at given time point.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 24, 52

End point values	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3	DTX401 Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3 <sup>[2]</sup>
Units: hours				
arithmetic mean (standard deviation)				
Change at Week 12; n=3, 3, 3, 0	3.3 ( $\pm 2.0$ )	1.7 ( $\pm 0.6$ )	1.4 ( $\pm 0.8$ )	99999 ( $\pm 99999$ )
Change at Week 24; n=3, 3, 3, 1	4.3 ( $\pm 4.2$ )	0.5 ( $\pm 0.6$ )	0.7 ( $\pm 1.7$ )	0.3 ( $\pm 999999$ )
Change at Week 52; n=3, 3, 2, 3	4.2 ( $\pm 2.2$ )	-1.8 ( $\pm 1.7$ )	-0.6 ( $\pm 0.1$ )	3.6 ( $\pm 2.7$ )

Notes:

[2] - 99999=NA (no participants assessed); 999999=NA (1 participant assessed)

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug (treatment emergent adverse events) through the End of Study/Early Withdrawal visit (up to Week 52) plus 30 days.

Adverse event reporting additional description:

Per protocol, serious events that occurred > 30 days after EOS or Early withdrawal visit, did not need to be reported unless Investigator considered them related to study product.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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### Reporting groups

Reporting group title	DTX401 Cohort 1
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Reporting group description:

DTX401 Dose 1 ( $2.0 \times 10^{12}$  GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)

Reporting group title	DTX401 Cohort 2
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Reporting group description:

DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation)

Reporting group title	DTX401 Cohort 3
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Reporting group description:

DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with an optimized reactive steroid regimen (7 weeks, at a starting dose of 60 mg/day, after ALT elevation)

Reporting group title	DTX401 Cohort 4
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Reporting group description:

DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with a prophylactic steroid regimen (8 weeks, at a starting dose of 60 mg/day, starting on Day 1)

Reporting group title	Total
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Reporting group description:

DTX401 Dose 1 ( $2.0 \times 10^{12}$  GC/kg) or DTX401 Dose 2 ( $6.0 \times 10^{12}$  GC/kg) with a reactive steroid regimen (6 weeks, at a starting dose of 40 mg/day, after ALT elevation), an optimized reactive steroid regimen (7 weeks, at a starting dose of 60 mg/day, after ALT elevation), or a prophylactic steroid regimen (8 weeks, at a starting dose of 60 mg/day, starting on Day 1)

Serious adverse events	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Lactic Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic Disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	DTX401 Cohort 4	Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Lactic Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
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: 0 %

Non-serious adverse events	DTX401 Cohort 1	DTX401 Cohort 2	DTX401 Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Face Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Hunger subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Thirst subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Immune system disorders Food Allergy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	2 / 3 (66.67%) 2
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Prostatitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oropharyngeal Pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Upper Respiratory Tract Congestion			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Libido Increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	0	2	3
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	3
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	4	1
Blood Creatinine Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood Glucose Fluctuation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Blood Uric Acid Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Heart Rate Increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hepatic Enzyme Increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2
Liver Function Test Increased subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 5	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Injury, poisoning and procedural complications			
Arthropod Bite subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Foot Fracture subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Muscle Strain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Stoma Site Discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Cardiac disorders			
Tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 8	2 / 3 (66.67%) 5	2 / 3 (66.67%) 4
Hypoaesthesia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Polycythaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	1	3	2
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Gastrointestinal Disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Malabsorption			



subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mouth Ulceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	2	2
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	1	3	3
Hepatobiliary disorders			
Hepatic Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dermatitis Acneiform			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hair Growth Abnormal			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0
Skin Striae subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Skin Ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Proteinuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1
Endocrine disorders Adrenal Insufficiency subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Adrenal Suppression subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Glucocorticoid Deficiency subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Back Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Gouty Arthritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint Noise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle Spasms			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Plantar Fasciitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abdominal Wall Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Covid-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal Viral Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Oral Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinobronchitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Tinea Pedis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	2	2
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	2
Lactic Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vitamin D Deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	DTX401 Cohort 4	Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	12 / 12 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Face Oedema			

subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Hunger			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Thirst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Prostatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Oropharyngeal Pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Rhinorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	1	3	
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Libido Increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 3 (66.67%)	6 / 12 (50.00%)	
occurrences (all)	7	12	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)	
occurrences (all)	0	6	
Blood Creatinine Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood Glucose Fluctuation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Blood Uric Acid Increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Heart Rate Increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	
Hepatic Enzyme Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 3	
Liver Function Test Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 12 (25.00%) 6	
Weight Decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Injury, poisoning and procedural complications Arthropod Bite subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Foot Fracture subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Muscle Strain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	
Stoma Site Discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Headache			



subjects affected / exposed	1 / 3 (33.33%)	8 / 12 (66.67%)	
occurrences (all)	1	18	
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	2 / 3 (66.67%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Polycythaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	5 / 12 (41.67%)	
occurrences (all)	0	6	
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Gastrointestinal Disorder			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Malabsorption			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mouth Ulceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)	
occurrences (all)	0	5	
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	5 / 12 (41.67%)	
occurrences (all)	0	7	
Hepatobiliary disorders			
Hepatic Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hypertransaminasaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 3 (66.67%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dermatitis Acneiform			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hair Growth Abnormal			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	2 / 3 (66.67%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Rash			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Skin Striae			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Skin Ulcer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	1	3	
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Endocrine disorders			
Adrenal Insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Adrenal Suppression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Glucocorticoid Deficiency			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Back Pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gouty Arthritis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Joint Noise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Muscle Spasms			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pain In Extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Plantar Fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Abdominal Wall Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Covid-19			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Folliculitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Gastrointestinal Viral Infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Hordeolum		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Influenza		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Nasopharyngitis		
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	2
Oral Candidiasis		
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)
occurrences (all)	1	1
Sinobronchitis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Sinusitis		
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	2
Tinea Pedis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Upper Respiratory Tract Infection		
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	3
Urinary Tract Infection		
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)
occurrences (all)	1	1
Viral Infection		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)	
occurrences (all)	5	9	
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 12 (25.00%)	
occurrences (all)	5	7	
Hypoglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)	
occurrences (all)	3	8	
Lactic Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vitamin D Deficiency			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2017	<ul style="list-style-type: none"> <li>Lactate testing was removed (except during the controlled fasting challenge).</li> <li>It was updated that subjects would be dosed at a minimum of 2 weeks (14 days) apart.</li> <li>Anti-G6Pase antibody testing was added as an exploratory objective and endpoint and as a safety assessment.</li> <li>The Week 2 visit was removed and an outpatient visit was added at Day 13.</li> <li>Exclusion criterion #8 was updated to exclude subjects based on the presence of, or history of treatment for, hepatitis B or hepatitis C.</li> <li>Previous genotyping results could be used to satisfy entry criteria.</li> <li>The definition of a dose-limiting toxicity was added.</li> <li>Sample size justification was added.</li> </ul>
02 March 2018	<ul style="list-style-type: none"> <li>Instructions for treating hypoglycemia after the controlled fasting challenge were added.</li> </ul>
18 February 2019	<ul style="list-style-type: none"> <li>The stopping criteria for the controlled fasting challenge was updated to include symptoms of hypoglycemia.</li> <li>An exploratory objective and endpoint were added to assess the impact of DTX401 on morning glucose levels. Corresponding assessments and analyses were added.</li> <li>A Morning Glucose Level worksheet was added.</li> <li>Use of cornstarch was updated from other analyses to efficacy analyses.</li> </ul>
10 September 2019	<ul style="list-style-type: none"> <li>The dosing interval for subjects after Cohort 2 was decreased to <math>\geq 1</math> week.</li> <li>The starting dose for reactive steroids was increased from 40 to 60 mg/day.</li> <li>The criterion for initiating steroids was modified to an increase in ALT compared to baseline or recently drawn levels.</li> <li>Language was added to allow consideration of steroid regimen modification if a subject's ALT levels do not normalize during the steroid taper.</li> <li>The target carbohydrate range of the prefasting challenge dinner meal was decreased to 15–20 g, and the prefasting challenge cornstarch dose was decreased to 5 g.</li> <li>Blood sample collection for measurement of glucose and lactate levels was added at the beginning of the fasting challenge to provide baseline levels.</li> <li>Symptoms of hypoglycemia was removed as a fasting challenge stopping criterion.</li> <li>Fasting challenge data to be captured in the eCRF was updated.</li> <li>Continuous glucose monitoring was added.</li> <li>The exploratory study objective and endpoint related to morning glucose level were modified to glucose level (due to the addition of continuous glucose monitoring).</li> <li>Measurement of lipid levels was added on the morning before the fasting challenge.</li> <li>Measurement of cortisol, fatty acid, glucagon, insulin, and ketone levels was added at the beginning and end of the fasting challenge.</li> <li>Measurement of cortisol levels was added <math>\sim 1</math> week before the Week 12 visit.</li> <li>The interval for liver function testing was decreased.</li> <li>Health-related quality of life assessments were added at Weeks 24 and 52.</li> <li>The Screening Period was increased from 42 to 56 days.</li> <li>The frequency of assessing prescribed diet/cornstarch and diet/cornstarch intake was increased to weekly.</li> <li>Measurement of weight was added at Weeks 6, 12, 24, and 36. Magnetic resonance imaging was moved from safety assessments to efficacy assessments.</li> </ul>

28 October 2019	<ul style="list-style-type: none"> <li>• Cohort 4 was added to assess a prophylactic oral steroid regimen for the prevention of vector-induced hepatitis after DTX401 administration.</li> <li>• Language was added to clarify that prescribed diet and diet intake should be assessed during scheduled study visits and, if possible, on a weekly basis for the duration of the study.</li> <li>• Language was added to clarify that prescribed cornstarch (or equivalent) and cornstarch (or equivalent) intake should be assessed during scheduled study visits and, if possible, on a weekly basis for the duration of the study.</li> <li>• Language was added to clarify that the CRM model would estimate the MTD of DTX401 regardless of the steroid approach used, reactive vs prophylactic.</li> </ul>
16 February 2021	<ul style="list-style-type: none"> <li>• The definition of euglycemia for the end of the controlled fasting challenge changed from <math>\geq 60</math> mg/dL (<math>\geq 3.33</math> mmol/L) to <math>\geq 54</math> mg/dL (<math>\geq 3.0</math> mmol/L).</li> <li>• The following changes were made to the controlled fasting challenge: <ul style="list-style-type: none"> <li>o CFC assessment was removed at Week 6 and optional at Week 12.</li> <li>o The composition of the dinner meal was updated to a personalized meal.</li> <li>o The prefasting cornstarch dose was updated to match the subject's most recent cornstarch prescription and timing after dinner.</li> <li>o Assessments at the beginning and end of the challenge were updated.</li> <li>o A final sample was added 30 minutes after the challenge.</li> <li>o Capillary glucose measurement was added.</li> </ul> </li> <li>• Week 6 was changed to an outpatient visit. Week 12 was changed from inpatient to outpatient (if the subject was still receiving prednisone at the time).</li> <li>• A new section was added to address the COVID-19 pandemic.</li> <li>• The definition of dose-limiting toxicity was revised to include events based on the Sponsor's evaluation of relatedness to DTX401, as well as the Investigator's.</li> <li>• A sample for ACTH assessment was added 1 week before the Week 12 visit.</li> </ul>

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported