



Clinical trial results:

Open-label, Long-term, Extension Treatment using Intra-Erythrocyte Dexamethasone Sodium Phosphate (EryDex System) in Patients with Ataxia Telangiectasia Who Participated in the ATTeST-IEDAT-02-2015 Study

Summary

EudraCT number	2018-000338-36
Trial protocol	ES DE BE PL GB NO IT
Global end of trial date	02 September 2022

Results information

Result version number	v1 (current)
This version publication date	10 May 2024
First version publication date	10 May 2024

Trial information

Trial identification

Sponsor protocol code	IEDAT-03-2018
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03563053
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 115929

Notes:

Sponsors

Sponsor organisation name	Erydel S.p.A.
Sponsor organisation address	Via Meucci, 3, Bresso, Italy, 20091
Public contact	Irene Maccabruni, Erydel S.p.A., imaccabruni@quincetx.com
Scientific contact	Irene Maccabruni , Erydel S.p.A., imaccabruni@quincetx.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 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2022
Global end of trial reached?	Yes
Global end of trial date	02 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective

To monitor and evaluate the long-term safety and tolerability of EDS-EP in AT patients.

Secondary Objective

To evaluate the long-term effect of EDS-EP on health-related Quality of Life (QoL; EQ-5D-5L scale).

Exploratory Objective:

To evaluate the long-term effect of EDS-EP in treating central nervous system (CNS) symptoms, as measured by the "Modified" International Cooperative Ataxia Rating Scale (mICARS), and Clinical Global Impression of severity and change (CGI-S/C).

Protection of trial subjects:

The study was conducted in accordance with the Helsinki Declaration and Good Clinical Practice. Any essential documents were archived as required by Good Clinical Practice and national regulations. Independent Ethics Committee approval and written informed consent were obtained prior to starting the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Tunisia: 7

Country: Number of subjects enrolled	India: 15
Country: Number of subjects enrolled	Australia: 2
Worldwide total number of subjects	104
EEA total number of subjects	44

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)	69
Adolescents (12-17 years)	6
Adults (18-64 years)	29
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of a total of 108 patients who completed the full treatment period in the ATTeST- IEDAT-02 study, 104 patients were enrolled in the IEDAT-03-2018 study and comprised the Total Set. These patients signed the ICF, completed the ATTeST study assessments, and did not present safety contraindications prior continuation with the EryDex treatment.

Pre-assignment

Screening details:

All patients enrolled in this study have participated in Study ATTeST-IEDAT-02-2015, and there was no de novo enrollment of new patients.

Patients meeting all selection criteria received monthly infusions of EDS-EP (dose range of ~14-22 mg DSP/infusion). If this dose of EDS-EP was not tolerated, the patient was discontinued from the study.

Period 1

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

Blinding implementation details:

It's a open label extension study, so no blinding was applicable.

Arms

Arm title	EryDex treatment
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Arm description:

~14-22 mg dexamethasone sodium phosphate (DSP) for 12 months. The duration of EryDex treatment could be extended further and continue until patients eventually withdrew consent, or the Investigator decided to discontinue treatment based on a risk / benefit assessment.

EryDex System was a combination product that was used to load DSP into autologous erythrocytes (EDS) creating the EDS-end product.

EryDex treatment consisted of a dose range correspondent to the ATTeST High Dose (obtained by loading 125 mg of DSP to the EryDex process and that, in the ATTeST, resulted in a mean of 17.4 ± 5.4 mg of DSP infused to patients) administered via ex vivo encapsulation into EDS that were infused into the patient with A-T. The dose of EryDex treatment was selected to allow collection of long-term safety data on the dose of erythrocyte encapsulated DSP that was considered more effective among the two different doses that were employed in the ATTeST study.

Arm type	Experimental
Investigational medicinal product name	EryDex System treatment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

EryDex treatment consisted of a dose range correspondent to the ATTeST High Dose (obtained by loading 125 mg of DSP to the EryDex process and that, in the ATTeST, resulted in a mean of 17.4 ± 5.4 mg (mean \pm standard deviation) of DSP infused to patients) administered via ex vivo encapsulation into EDS that were infused into the patient with A-T. EryDex treatment was administered monthly throughout the period of the study. The duration of EryDex treatment was planned for 12 months but could be extended further and continue until patients eventually withdrew consent, or the Investigator decided to discontinue treatment based on a risk / benefit assessment.

Number of subjects in period 1	EryDex treatment
Started	104
Total Set	104
Safety Set	104
Full Analysis Set	80
Month 12	64
Month 24	33
Month 36	21
Month 48	7
Month 57	1
Completed	0
Not completed	104
Consent withdrawn by subject	17
Physician decision	1
Adverse event, non-fatal	3
Study terminated by the sponsor	71
Due to the COVID-19 pandemic	12

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)
Reporting group description: -	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	104	104	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	69	69	
Adolescents (12-17 years)	6	6	
Adults (18-64 years)	29	29	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	11.4		
standard deviation	± 4.57	-	
Gender categorical Units: Subjects			
Female	55	55	
Male	49	49	

Subject analysis sets

Subject analysis set title	EryDex - FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set Population (FAS): the FAS comprised all patients who entered IEDAT-03-2018 study, had a Baseline Efficacy Assessment in IEDAT-03-2018 and who received at least one dose of study medication and had at least one post-Baseline Efficacy Assessment of the ICARS in this extension study.

Subject analysis set title	EryDex - Total Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In this trial, the Total or Overall Set (N=104) numerically corresponds to the Safety set, which included all patients who provided informed consent or assent and who received any dose of study medication during ATTeST-IEDAT-03-2018 study (i.e., "Date performed" given on the "EDS-EP Infusion" eCRF page at any Visit).

Subject analysis set title	EryDex - SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consisted of all patients who provided informed consent or assent and who received any dose of study medication during IEDAT-03-2018 study. The Safety Analysis Set was used for all safety analyses.

Reporting group values	EryDex - FAS	EryDex - Total Set	EryDex - SAF
Number of subjects	80	104	104
Age categorical			
Units: Subjects			
In utero		0	0
Preterm newborn infants (gestational age < 37 wks)		0	0
Newborns (0-27 days)		0	0
Infants and toddlers (28 days-23 months)		0	0
Children (2-11 years)		69	69
Adolescents (12-17 years)		6	6
Adults (18-64 years)		29	29
From 65-84 years		0	0
85 years and over		0	0
Age continuous			
Units: years			
arithmetic mean		11.4	11.4
standard deviation	±	± 4.57	± 4.57
Gender categorical			
Units: Subjects			
Female		55	55
Male		49	49

End points

End points reporting groups

Reporting group title	EryDex treatment
Reporting group description: ~14-22 mg dexamethasone sodium phosphate (DSP) for 12 months. The duration of EryDex treatment could be extended further and continue until patients eventually withdrew consent, or the Investigator decided to discontinue treatment based on a risk / benefit assessment. EryDex System was a combination product that was used to load DSP into autologous erythrocytes (EDS) creating the EDS-end product. EryDex treatment consisted of a dose range correspondent to the ATTeST High Dose (obtained by loading 125 mg of DSP to the EryDex process and that, in the ATTeST, resulted in a mean of 17.4 ± 5.4 mg of DSP infused to patients) administered via ex vivo encapsulation into EDS that were infused into the patient with A-T. The dose of EryDex treatment was selected to allow collection of long-term safety data on the dose of erythrocyte encapsulated DSP that was considered more effective among the two different doses that were employed in the ATTeST study.	
Subject analysis set title	EryDex - FAS
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis Set Population (FAS): the FAS comprised all patients who entered IEDAT-03-2018 study, had a Baseline Efficacy Assessment in IEDAT-03-2018 and who received at least one dose of study medication and had at least one post-Baseline Efficacy Assessment of the ICARS in this extension study.	
Subject analysis set title	EryDex - Total Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: In this trial, the Total or Overall Set (N=104) numerically corresponds to the Safety set, which included all patients who provided informed consent or assent and who received any dose of study medication during ATTeST-IEDAT-03-2018 study (i.e., "Date performed" given on the "EDS-EP Infusion" eCRF page at any Visit).	
Subject analysis set title	EryDex - SAF
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Analysis Set consisted of all patients who provided informed consent or assent and who received any dose of study medication during IEDAT-03-2018 study. The Safety Analysis Set was used for all safety analyses.	

Primary: Number of Treatment-Emergent Adverse Event (TEAE), treatment-emergent serious adverse events (TESAE), and adverse events of special interest (AESI) throughout the study

End point title	Number of Treatment-Emergent Adverse Event (TEAE), treatment-emergent serious adverse events (TESAE), and adverse events of special interest (AESI) throughout the study ^[1]
End point description: Assessment of TEAEs, treatment-emergent serious adverse events (TESAE), and adverse events of special interest (AESI) were performed throughout the study, from the time of signing of the ICF at Baseline Visit through to the Final Study Visit (Month 12 or early discontinuation). All patients were to be followed up through 30 days after the Final Visit (Month 12 or early discontinuation) or at least 60 days after the final infusion, whichever was longer.	
End point type	Primary
End point timeframe: From Baseline (Visit 1 - Day 0) to Follow-up (~60 days after last infusion)	
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: Not applicable.	

End point values	EryDex - SAF			
Subject group type	Subject analysis set			
Number of subjects analysed	104			
Units: Number of events				
number (not applicable)				
Number of TEAEs	1233			
Number of Serious TEAEs	19			
Number of TEAE leading to Death	0			
Number of TEAE leading to Permanent Withdrawal of	5			
Adverse Events During COVID-19 Interruption - On D	3			
Adverse Events During COVID-19 Interruption - Off	3			
Adverse Events During COVID-19 Interruption - Rest	55			
TEAE by Worst Intensity - Mild	1029			
TEAE by Worst Intensity - Moderate	187			
TEAE by Worst Intensity - Severe	17			
TEAE by Closest Relationship to Treatment - Probab	283			
TEAE by Closest Relationship to Treatment - Possib	167			
TEAE by Closest Relationship to Treatment - Unlike	178			
TEAE by Closest Relationship to Treatment - Not re	604			
Number of AESI	83			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life Using EQ-5D-5L Scale to Month 54

End point title	Change From Baseline in Quality of Life Using EQ-5D-5L Scale to Month 54
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End point description:

The EQ-5D included single item measures of 5 health dimensions:

- mobility,
- self-care,
- usual activities,
- pain / discomfort, and
- anxiety / depression.

In addition, EQ-5D included a global rating of current health using a visual analogue scale (VAS) ranging from 0 (worst health imaginable) to 100 (best health imaginable). The EQ VAS provided a quantitative measure of the patient's perception of their overall health.

The EQ-5D-5L included five levels of severity (i.e., no problems, slight problems, moderate problems, severe problems, and extreme problems) for each of the five EQ-5D dimensions. These levels were scored from 1 = no problems to 5 = extreme problems: from 5, min/worst, to 25, best/max); EQ-VAS (EQ Visual Analogue scale) scoring from 0, min/worst, to 100, best/max. The efficacy data focus mainly up to Month 36 as afterwards the number of patients / assessments dropped below 20% of the initial sample size, which was required for the efficacy evaluations.

End point type	Secondary
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End point timeframe:

From Baseline (Visit 1- Day 0) to Month 36

End point values	EryDex - FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	80 ^[2]			
Units: Score on a scale				
arithmetic mean (standard deviation)				
to Month 6	0.015 (± 0.1131)			
to Month 12	-0.022 (± 0.1145)			
to Month 18	0.007 (± 0.1233)			
to Month 24	0.011 (± 0.1746)			
to Month 30	-0.021 (± 0.1117)			
to Month 36	0.011 (± 0.1242)			

Notes:

[2] - Month 6 N=73, Month 12 N=61, Month 18 N=51, Month 24 N=32, Month 30 N=22, Month 36 N=20

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Improving, Stable or Worsening Score Using a Clinical Global Impression of Change (CGI-C) From Baseline (Visit 1- Day 0) to Month 54

End point title	Number of Patients With Improving, Stable or Worsening Score Using a Clinical Global Impression of Change (CGI-C) From Baseline (Visit 1- Day 0) to Month 54
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End point description:

The CGI-C scale assesses the change in the patient's clinical status from baseline using a 7-point scale, ranging from 1 (very much improved) to 7 (very much worse), with a score of 4 indicating no change. Clinicians were required to conduct a full clinical interview and examination of the patient.

The interview and examination assessed various aspects of the patient's appearance (grooming, evidence of falls, etc.), ataxia, cognition (orientation, calculation ability, language, ability to follow commands, memory, etc.), apraxia, dysarthria, extrapyramidal motor symptoms, activities of daily living, and mood. The higher the score the worse the outcome.

The efficacy data focus mainly up to Month 36 as afterwards the number of patients / assessments dropped below 20% of the initial sample size, which was required for the efficacy evaluations.

End point type	Secondary
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End point timeframe:

From Baseline (Visit 1- Day 0) to Month 36

End point values	EryDex - FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	80 ^[3]			
Units: Number of Patients				
number (not applicable)				
Month 6 - Improved (Score 1-3)	9			
Month 6 - No change or Worsened (Score 4-7)	68			
Month 12 - Improved (Score 1-3)	14			
Month 12 - No change or Worsened (Score 4-7)	45			
Month 18 - Improved (Score 1-3)	6			
Month 18 - No change or Worsened (Score 4-7)	41			
Month 24 - Improved (Score 1-3)	5			
Month 24 - No change or Worsened (Score 4-7)	26			
Month 30 - Improved (Score 1-3)	2			
Month 30 - No change or Worsened (Score 4-7)	17			
Month 36 - Improved (Score 1-3)	3			
Month 36 - No change or Worsened (Score 4-7)	16			

Notes:

[3] - Month 6 N=80, Month 12 N=59, Month 18 N=47, Month 24 N=29, Month 30 N=19, Month 36 N=19

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With None to Severe (0 to 4) Scores in Clinical Global Impression of Severity (CGI-S)-Structured of Neurological Symptoms of AT From Baseline (Visit 1 - Day 0) to Month 54

End point title	Number of Patients With None to Severe (0 to 4) Scores in Clinical Global Impression of Severity (CGI-S)-Structured of Neurological Symptoms of AT From Baseline (Visit 1 - Day 0) to Month 54
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End point description:

The CGI-S scale measures global severity of illness at a given point in time, and is usually rated on a 7-point, Likert-type scale ranging from 1 (normal, not ill at all) to 7 (among the most extremely ill patients). No version of the CGI-S exists which has been specifically adapted for use in patients with A-T; therefore, a 5-point version was developed that considered the severity of the following symptoms of A-T: ataxia (walking), dysarthria, dysmetria, extrapyramidal symptoms (chorea, myoclonus, dystonia, and tremor), and eye movements. Ratings of none (0), mild (1), moderate (2), severe (3), and very severe (4) were selected based on the level of symptomatology. The higher the score the worse the outcome.

The efficacy data focus mainly up to Month 36 as afterwards the number of patients / assessments dropped below 20% of the initial sample size, which was required for the efficacy evaluations.

End point type	Secondary
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End point timeframe:

From Baseline (Visit 1- Day 0) to Month 36

End point values	EryDex - FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	80 ^[4]			
Units: Number of Patients				
number (not applicable)				
Baseline - CGI-S Score - 0	2			
Baseline - CGI-S Score - 1	18			
Baseline - CGI-S Score - 2	31			
Baseline - CGI-S Score - 3	23			
Baseline - CGI-S Score - 4	0			
Month 6 - CGI-S Score - 0	1			
Month 6 - CGI-S Score - 1	20			
Month 6 - CGI-S Score - 2	30			
Month 6 - CGI-S Score - 3	22			
Month 6 - CGI-S Score - 4	3			
Month 12 - CGI-S Score - 0	0			
Month 12 - CGI-S Score - 1	12			
Month 12 - CGI-S Score - 2	28			
Month 12 - CGI-S Score - 3	17			
Month 12 - CGI-S Score - 4	2			
Month 18 - CGI-S Score - 0	0			
Month 18 - CGI-S Score - 1	13			
Month 18 - CGI-S Score - 2	21			
Month 18 - CGI-S Score - 3	12			
Month 18 - CGI-S Score - 4	1			
Month 24 - CGI-S Score - 0	0			
Month 24 - CGI-S Score - 1	10			
Month 24 - CGI-S Score - 2	10			
Month 24 - CGI-S Score - 3	9			
Month 24 - CGI-S Score - 4	2			
Month 30 - CGI-S Score - 0	0			
Month 30 - CGI-S Score - 1	5			
Month 30 - CGI-S Score - 2	10			
Month 30 - CGI-S Score - 3	4			
Month 30 - CGI-S Score - 4	0			
Month 36 - CGI-S Score - 0	0			
Month 36 - CGI-S Score - 1	3			
Month 36 - CGI-S Score - 2	10			
Month 36 - CGI-S Score - 3	6			
Month 36 - CGI-S Score - 4	0			

Notes:

[4] - Baseline N=74, Month 6 N=76, Month 12 N=59, Month 18 N=47, Month 24 N=31, Month30 N=19, Month36 N= 19

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline of the Modified International Cooperative Ataxia Rating Scale (mICARS) until month 54

End point title	Change from baseline of the Modified International Cooperative Ataxia Rating Scale (mICARS) until month 54
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End point description:

The International Cooperative Ataxia Rating Scale (ICARS) was an assessment of the degree of impairment in patients with cerebellar ataxia and was administered in its entirety; however, the primary efficacy assessment was based on the modified (m)ICARS, which excluded the Oculomotor domain (items 17 to 19) and items 8 to 12 of the Kinetic Functions domain of the ICARS. The mICARS was a 54 points maximum score (min 0) questionnaire divided into 3 sections:

- Posture and Gait Disturbance section-7 items (min score 0, max score 34)
- Kinetic Function-2 items (min 0, max 12)
- Speech Disorder- 2 items (min 0, max 8).

An higher scores - both for total and subscores - indicate a higher level of disease impairment. The subscores are added to give the total score.

The efficacy data focus mainly up to Month 36 as afterwards the number of patients / assessments dropped below 20% of the initial sample size, which was required for the efficacy evaluations.

End point type	Secondary
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End point timeframe:

From Baseline (Visit 1- Day 0) to Month 36

End point values	EryDex - FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	80 ^[5]			
Units: Score on a scale				
arithmetic mean (standard deviation)				
to Month 6	0.7 (± 4.09)			
to Month 12	1.5 (± 3.36)			
to Month 18	2.7 (± 4.28)			
to Month 24	3.9 (± 4.96)			
to Month 30	4.5 (± 5.41)			
to Month 36	34.0 (± 5.17)			

Notes:

[5] - Month 6 N=78, Month 12 N=60, Month 18 N=48, Month 24 N=32, Month 30 N=21, Month 36 N=18

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were all the AEs reported from Baseline (Visit 1 - Day 0) to Follow-up (~60 days after the last infusion).

Adverse event reporting additional description:

All AEs that occurred during this IEDAT-03-2018 study are defined as TEAEs, as all patients received EryDex treatment in the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	EryDex - SAF
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Reporting group description:

The Safety Analysis Set consisted of all patients who provided informed consent or assent and who received any dose of study medication during IEDAT-03-2018 study. The Safety Analysis Set was used for all safety analyses.

Serious adverse events	EryDex - SAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 104 (11.54%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hodgkin's disease			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Odontogenic cyst			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Forearm fracture			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Gastrointestinal tube insertion			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngeal swelling			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Trombocytopenic Purpura			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lower respiratory tract infection			

subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	EryDex - SAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 104 (94.23%)		
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences (all)	8		
Coronavirus test positive			
subjects affected / exposed	7 / 104 (6.73%)		
occurrences (all)	8		
Serum ferritin decreased			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences (all)	9		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences (all)	10		
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed occurrences (all) Infusion related reaction subjects affected / exposed occurrences (all)	7 / 104 (6.73%) 10 28 / 104 (26.92%) 199		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	15 / 104 (14.42%) 22		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	6 / 104 (5.77%) 9		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	16 / 104 (15.38%) 20 33 / 104 (31.73%) 54		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	23 / 104 (22.12%) 32 7 / 104 (6.73%) 9 20 / 104 (19.23%) 38		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis	19 / 104 (18.27%) 42		

subjects affected / exposed occurrences (all)	7 / 104 (6.73%) 10		
Rhinorrhoea subjects affected / exposed occurrences (all)	12 / 104 (11.54%) 17		
Skin and subcutaneous tissue disorders			
Erythema subjects affected / exposed occurrences (all)	7 / 104 (6.73%) 10		
Pruritus subjects affected / exposed occurrences (all)	7 / 104 (6.73%) 7		
Rash subjects affected / exposed occurrences (all)	9 / 104 (8.65%) 11		
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	10 / 104 (9.62%) 15		
Corona Virus Infection subjects affected / exposed occurrences (all)	17 / 104 (16.35%) 19		
Nasopharyngitis subjects affected / exposed occurrences (all)	21 / 104 (20.19%) 30		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	23 / 104 (22.12%) 36		
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 104 (5.77%) 7		
Product issues			
Product contamination subjects affected / exposed occurrences (all)	13 / 104 (12.50%) 19		
Metabolism and nutrition disorders			

Iron deficiency subjects affected / exposed occurrences (all)	16 / 104 (15.38%) 29		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2018	<ul style="list-style-type: none">• Revision of the study procedures to ensure that sterility is maintained throughout the collection of autologous blood cells, processing, administration, and testing (rapid testing, gram stain and culture) of EryDex treatment.• Addition of the reference to the document entitled "Study Procedures on Sterility Testing for Study IEDAT-03-2018 (Open Label Extension (OLE)-IEDAT)".• Minor editorial changes have been made and additional clarifications provided, including a modification in the study's entry criteria to allow inclusion of patients that have not worsened significantly on treatment.
30 April 2018	<ul style="list-style-type: none">• Provision of clarification explaining that the Principal Investigator, instead of the CRO, will decide if a patient is eligible to continue into the IEDAT-03-2018 study.• The removal of requirement that the patient cannot worsen significantly during treatment (e.g., evidence of disease stabilisation or improvement as determined by the ratings of the CGI-C) to be eligible for the IEDAT-03-2018 study, to avoid doubts regarding the exclusion of the placebo patients who might not show disease stabilisation or improvement. Therefore, it has been clarified that, to be eligible for the IEDAT-03-2018 study, patients must have completed 12 months of treatment in the ATTeST study, including all its study assessments, do not present safety contraindication to continuation of treatment, and provide informed consent.
19 March 2019	<ul style="list-style-type: none">• CRO references were changed.• Safety e-mail was changed.• EryDel address was updated on the Sample Study Solutions and Medication Labels.
29 April 2019	<ul style="list-style-type: none">• In the study design, the treatment period was changed from 12 months of treatment to full treatment period.• During the study, Long-term Efficacy Assessments were changed from a 6-month frequency to approximately every 6 months.• Rapid microbial detection test (Staining test) was removed.• The definition of the allowed treatment window was clarified: the monthly infusions should be performed every 21-28 days. A window of + 10 days was permitted for each of the scheduled Monthly Visits. Therefore, no EDS-EP infusion should be performed less than 21 days or more than 38 days after the previous infusion. The window between an infusion and the subsequent one should be kept as regular as possible throughout the study, avoiding fluctuations in administration windows. The date of an infusion is not bound to the date of the initial treatment but to the date of the previous IMP administration.• Exclusion Criterion #4 was changed and a value in case of oral candidiasis was added. More in details:<ul style="list-style-type: none">- PREVIOUS version: CD4+ lymphocyte count < 400 / mm³ (for patients 6 years of age) or < 200 / mm³ (for patients > 6 years).- UPDATED version: CD4+ lymphocyte count < 400 / mm³ (for patients 6 years of age) or < 150 / mm³ (for patients > 6 years). In presence of oral infections, like oral candidiasis, documented at the screening or recurrent as per medical history documentation, the limit increases to < 200 / mm³ (for patients > 6 years).• The Microbial Staining test was removed.

22 May 2020	<ul style="list-style-type: none"> • The planned number of patients was updated to 155. • Timelines for the last patient in were updated. • Appendix 13 was added: Temporary changes to the Protocol implemented / to be implemented because of COVID-19 pandemic.
01 December 2020	<ul style="list-style-type: none"> • Study design and rationale were updated to allow patients who were discontinued from the ATTeST study during the COVID-19 pandemic to receive the EryDex treatment in the context of the IEDAT-03-2018 study. • Inclusion criterion #1 was revised to include patients discontinued the ATTEST study during the COVID-19 pandemic. • Visit assessments and schedule were amended to reflect the updated study design and inclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

India was particularly affected by COVID-19-dependent treatment and visit interruptions. This long interruption would have resulted in insufficient long-term safety data. For this reason, EryDel decided to discontinue the IEDAT-03-2018 study in India

Notes: