Clinical trial results:
Evaluation of Effects of Intra-Erythrocyte Dexamethasone Sodium Phosphate on Neurological Symptoms in Ataxia-Teleangectasia Patients

Summary

EudraCT number	2010-022315-19
Trial protocol	IT
Global end of trial date	31 August 2011

Results information

Result version number	v1 (current)
This version publication date	11 June 2022
First version publication date	11 June 2022

Trial information

Trial identification

Sponsor protocol code	IEDAT-ERY01-2010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01255358
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Erydel S.p.A.
Sponsor organisation address	Via Meucci, 3, Bresso (MI), Italy, 20091
Public contact	Clinical Trial Transparency Manager, Erydel S.p.A., +39 02 36504470, info@erydel.com
Scientific contact	Clinical Trial Transparency Manager, Erydel S.p.A., +39 02 36504470, info@erydel.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	31 August 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2011
Global end of trial reached?	Yes
Global end of trial date	31 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the improvement in central nervous system (CNS) symptoms measured by International Co-operative Ataxia Rating Scale (ICARS) in patients with Ataxia-Teleangectasia (AT), during a period of treatment with ERY-DEX (dexamethasone sodium phosphate ex vivo encapsulated into human autologous erythrocytes).

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000 - Notes of Clarification on Paragraph 29 added by the World Medical Association (WMA) General Assembly, Washington 2002 and on Paragraph 30 added by the WMA General Assembly, Tokyo 2004) and that are consistent with International Conference on Harmonization (ICH)/GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	15
Adolescents (12-17 years)	5
Adults (18-64 years)	2

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twenty-two patients were enrolled: 18 patients completed the study while there were four dropouts/withdrawals during the study period.

Pre-assignment

Screening details:

A total of 26 patients were screened at the two centers involved in the study. Only 22 patients were enrolled in the study.
Of the 26 patients screened, four were screening failures (three for low levels of CD4+ lymphocytes and one for concomitant disease disallowed by the protocol).

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:

The study was non-blinded since IEDAT-ERY01-2010 was an open-label study.

Arms

Arm title	EryDex

Arm description:

Six-month monthly treatment with Ery-Dex (dexamethasone sodium phosphate encapsulated in autologous erythrocytes).
Patients received intravenous infusion of 50 ml of autologous erythrocytes engineered to contain dexamethasone sodium phosphate encapsulated into erythrocytes that was previously taken from the same patient.

Arm type	Experimental
Investigational medicinal product name	EryDex
Investigational medicinal product code	
Other name	dexamethasone sodium phosphate
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone sodium phosphate encapsulated in human erythrocytes (Er-Dex): two vials of 250 mg/10 ml each.
Patients received intravenous infusion of dexamethasone sodium phosphate (final amount about 10-15 mg) ex vivo encapsulated into autologous erythrocytes (2 vials of 250 mg each of dexamethasone sodium phosphate were used in the ex vivo process together with 50 ml of blood). The treatment was repeated at intervals of 30 days (±10 days), for a total of 6 infusions.

Number of subjects in period 1	EryDex
Started	22
Completed	18
Not completed	4
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	EryDex

Reporting group description:

Six-month monthly treatment with Ery-Dex (dexamethasone sodium phosphate encapsulated in autologous erythrocytes).
Patients received intravenous infusion of 50 ml of autologous erythrocytes engineered to contain dexamethasone sodium phosphate encapsulated into erythrocytes that was previously taken from the same patient.

Reporting group values	EryDex	Total	
Number of subjects	22	22	
Age categorical			
Units: Subjects			
Children (2-11 years)	15	15	
Adolescents (12-17 years)	5	5	
Adults (18-64 years)	2	2	
Age continuous			
Units: years			
arithmetic mean	11.2		
standard deviation	± 3.5	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	11	11	

Subject analysis sets

Subject analysis set title	EryDex - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex.

Subject analysis set title	EryDex - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP Population included patients who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Visit 1 (Baseline) population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 1 (baseline) population - PP
Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients
who were treated according to protocol and fulfilled the following criteria:

• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Visit 4 population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 7 population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 4 population - PP
Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation]

Subject analysis set title	Visit 7 population - PP
Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Screening population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population includes all 22 patients enrolled into the study.

Reporting group values	EryDex - ITT population	EryDex - PP population	Visit 1 (Baseline) population - ITT
Number of subjects	22	18	22
Age categorical Units: Subjects			
Children (2-11 years)	15	12	15
Adolescents (12-17 years)	5	4	5
Adults (18-64 years)	2	2	2
Age continuous Units: years			
arithmetic mean	11.2		
standard deviation	± 3.5	±	±
Gender categorical Units: Subjects			
Female	11	8	
Male	11	10	

Reporting group values	Visit 1 (baseline) population - PP	Visit 4 population - ITT	Visit 7 population - ITT
Number of subjects	18	19	22

Age categorical Units: Subjects			
Children (2-11 years)	12		
Adolescents (12-17 years)	4		
Adults (18-64 years)	2		
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			
Male			

Reporting group values	Visit 4 population - PP	Visit 7 population - PP	Screening population
Number of subjects	18	18	22
Age categorical Units: Subjects			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	EryDex

Reporting group description:

Six-month monthly treatment with Ery-Dex (dexamethasone sodium phosphate encapsulated in autologous erythrocytes).
Patients received intravenous infusion of 50 ml of autologous erythrocytes engineered to contain dexamethasone sodium phosphate encapsulated into erythrocytes that was previously taken from the same patient.

Subject analysis set title	EryDex - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex.

Subject analysis set title	EryDex - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP Population included patients who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Visit 1 (Baseline) population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT Population included all patients enrolled into the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 1 (baseline) population - PP
Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients
who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Visit 4 population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into
the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 7 population - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population included all patients enrolled into
the study, who received at least one infusion of EryDex

Subject analysis set title	Visit 4 population - PP
Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients
who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation]

Subject analysis set title	Visit 7 population - PP

Subject analysis set type	Per protocol

Subject analysis set description:

PP Population included patients
who were treated according to protocol and fulfilled the following criteria:
• compliance with all entry criteria
• absence of major protocol violations
• adequate compliance with trial medication [at most one missed or untimely (outside the allowable ±10 days time-window) infusion of the study preparation].

Subject analysis set title	Screening population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population includes all 22 patients enrolled into the study.

Primary: Change from baseline in mean ICARS Total score by visit

End point title	Change from baseline in mean ICARS Total score by visit

End point description:

Changes in neurological symptoms were assessed using the International Co-operative Ataxia Rating Scale (ICARS), which is a semiquantitative scale offering a compartmentalized quantification of the following 4 subscores: Posture and Gait Disturbances
(maximum score = 34), Kinetic Functions (maximum score = 52), Speech Disorders (maximum score = 8), and Oculomotor Disorders (maximum score = 6), for a possible total score of 100 points (higher score corresponds to worse status)
Changes in ICARS scores were calculated for each patient by subtracting the score at V1 from the score at each of the
follow-up visits.

End point type	Primary

End point timeframe:

At Visit 2 (Day 30), 4 (Day 90), 7 (Day 180)

End point values	EryDex - ITT population	EryDex - PP population	Visit 1 (Baseline) population - ITT	Visit 1 (baseline) population - PP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[1]	18	22	18
Units: score				
arithmetic mean (standard deviation)				
Visit 2	-2.2 (± 5.6)	-2.4 (± 4.9)	000 (± 000)	000 (± 000)
Visit 4	-3.7 (± 7.3)	-3.9 (± 7.1)	000 (± 000)	000 (± 000)
Visit 7	-4.0 (± 7.5)	-5.2 (± 7.0)	000 (± 000)	000 (± 000)

Notes:

[1] - At Visit 4 N=19

Statistical analyses

Statistical analysis title	Visit 2 vs Visit 1 (baseline)
Comparison groups	EryDex - ITT population v Visit 1 (Baseline) population - ITT

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.107
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 4 vs Visit 1 (baseline)
Comparison groups	EryDex - ITT population v Visit 1 (Baseline) population - ITT
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.054
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed since the overall analysis was significant comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 7 vs Visit 1 (baseline)
Comparison groups	EryDex - ITT population v Visit 1 (Baseline) population - ITT
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.024
Method	Wilcoxon (Mann-Whitney)

Notes:

[4] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed since the overall analysis was significant comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 2 vs Visit 1 (baseline)
Comparison groups	EryDex - PP population v Visit 1 (baseline) population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.059
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed since the overall analysis was significant comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 4 vs Visit 1 (baseline)
Comparison groups	EryDex - PP population v Visit 1 (baseline) population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.032
Method	Wilcoxon (Mann-Whitney)

Notes:

[6] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed since the overall analysis was significant comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 7 vs Visit 1 (baseline)
Comparison groups	EryDex - PP population v Visit 1 (baseline) population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.01
Method	Wilcoxon (Mann-Whitney)

Notes:

[7] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
Changes over time in the ICARS Total score were analyzed with a Repeated Measures Analysis of Variance (RMANOVA) with possible covariates (e.g. age and ICARS at baseline). A Wilcoxon non-parametric test evaluating changes between visits was performed since the overall analysis was significant comparing V4 and V7 compared to baseline (V1).

Secondary: Mean Investigator Global Assessment (IGA) by visit

End point title	Mean Investigator Global Assessment (IGA) by visit

End point description:

The IGA consisted of an evaluation of neurological signs and symptoms defined as neuromotor disorders, posture and deambulation, disturbances of the oro-pharyngeal apparatus, presence of peripheral neuropathy, neurodevelopmental disturbances, intellectual level, and behavior disturbances, which was based only on a subjective judgment of the Investigator.
A 5 point qualitative scale with rating categories of "very much improved (1), slightly improved (2) no change (3),
slightly worsened (4), and very much worsened (5)" was used to assess changes at V4 and V7, compared
to the patient's condition at baseline.

End point type	Secondary

End point timeframe:

At Visit 4 and Visit 7

End point values	Visit 4 population - ITT	Visit 7 population - ITT	Visit 4 population - PP	Visit 7 population - PP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	22	18	18
Units: score				
arithmetic mean (standard deviation)	2.2 (± 0.9)	2.4 (± 0.8)	2.0 (± 0.8)	2.2 (± 0.7)

Statistical analyses

Statistical analysis title	Visit 7 vs Visit 4
Comparison groups	Visit 4 population - ITT v Visit 7 population - ITT
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.44
Method	Wilcoxon (Mann-Whitney)

Notes:

[8] - This is a within-arm comparison: groups examined should not be added. N=41 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test has been conducted on both ITT and PP Populations by comparing V4 vs. V7 scores.

Statistical analysis title	Visit 7 vs Visit 4
Comparison groups	Visit 4 population - PP v Visit 7 population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	= 0.157
Method	Wilcoxon (Mann-Whitney)

Notes:

[9] - This is a within-arm comparison: groups examined should not be added. N=36 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test has been conducted on both ITT and PP Populations by comparing V4 vs. V7 scores.

Secondary: Ocular motility by visit

End point title	Ocular motility by visit

End point description:

Changes vs. baseline were computed through a 5-point qualitative scale as: "very much improved, slightly improved, no change, slightly worsened, very much worsened" (The Investigator will state if the condition was very much improved, slightly improved, exhibited no change, was slightly worse or very much worse).

End point type	Secondary

End point timeframe:

At Visit 4 and at Visit 7

End point values	Visit 4 population - ITT	Visit 7 population - ITT	Visit 4 population - PP	Visit 7 population - PP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	22	18	18
Units: score				
arithmetic mean (standard deviation)	2.6 (± 0.7)	2.4 (± 0.7)	2.6 (± 0.7)	2.2 (± 0.7)

Statistical analyses

Statistical analysis title	Visit 7 vs Visit 4
Comparison groups	Visit 4 population - ITT v Visit 7 population - ITT
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.014
Method	Wilcoxon (Mann-Whitney)

Notes:

[10] - This is a within-arm comparison: groups examined should not be added. N=41 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test has been conducted on both ITT and PP Populations by comparing V4 vs. V7 scores.

Statistical analysis title	Visit 7 vs Visit 4
Comparison groups	Visit 4 population - PP v Visit 7 population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.014
Method	Wilcoxon (Mann-Whitney)

Notes:

[11] - This is a within-arm comparison: groups examined should not be added. N=36 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test has been conducted on both ITT and PP Populations by comparing V4 vs. V7 scores.

Secondary: Change from baseline in Vineland Adaptive Behaviour Scale (VABS) by visit

End point title	Change from baseline in Vineland Adaptive Behaviour Scale (VABS) by visit

End point description:

The VABS complete form consists of 540 items, 261 of which were taken from the short form, and is administered by a semistructured interview by a trained interviewer with a parent or operator who takes care of the patient. The adaptive behaviour is measured according to four scales, each subdivided into eleven subscales. Each subscale is further divided into clusters (2 to 8 items) listed in evolutionary order; each cluster is sorted to a target item. A score can be assigned to the items: this score is intended to indicate whether the subjects perform that activity “usually”, “sometimes” or “never”; answers as “no chance” or “I do not know” are also provided.
Scales and Subscales. VABS are divided into four scales and eleven subscales: 1) Communication: Receptive, Expressive, Written; 2) Daily Living Skills: Personal, Domestic, Community; 3) Socialization: Interpersonal Relationships, Play & Leisure Time, Coping Skills; 4) Motor Skills: Gross, Fine.

End point type	Secondary

End point timeframe:
At Visit 4 (Day 90) and Visit 7 (Day 180).

End point values	EryDex - ITT population	EryDex - PP population	Visit 1 (Baseline) population - ITT	Visit 1 (baseline) population - PP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[12]	18	22	18
Units: score				
arithmetic mean (standard deviation)				
Visit 4	1.0 (± 0.9)	1.1 (± 0.9)	000 (± 000)	000 (± 000)
Visit 7	1.3 (± 1.2)	1.5 (± 1.1)	000 (± 000)	000 (± 000)

Notes:
[12] - At visit 4 N=19

Statistical analyses

Statistical analysis title	Visit 4 vs Visit 1 (baseline)
Comparison groups	EryDex - ITT population v Visit 1 (Baseline) population - ITT
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:
[13] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test was performed comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 7 vs Visit 1 (baseline)
Comparison groups	Visit 1 (Baseline) population - ITT v EryDex - ITT population
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:
[14] - This is a within-arm comparison: groups examined should not be added. N=44 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test was performed comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 4 vs Visit 1 (baseline)
Comparison groups	EryDex - PP population v Visit 1 (baseline) population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:

[15] - This is a within-arm comparison: groups examined should not be added. N=36 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test was performed comparing V4 and V7 compared to baseline (V1).

Statistical analysis title	Visit 7 vs Visit 1 (baseline)
Comparison groups	EryDex - PP population v Visit 1 (baseline) population - PP
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:

[16] - This is a within-arm comparison: groups examined should not be added. N=36 is an innate error of the EudraCT database system.
A Wilcoxon non-parametric test was performed comparing V4 and V7 compared to baseline (V1).

Secondary: Hematology values by visit

End point title	Hematology values by visit

End point description:

Absolute values are reported.

End point type	Secondary

End point timeframe:

At screening and at Visit 7

End point values	Visit 7 population - ITT	Screening population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: units				
arithmetic mean (standard deviation)				
hemoglobin (g/dl)	12.8 (± 1.0)	13.5 (± 0.9)		
hematocrit (%)	39.0 (± 3.0)	41.0 (± 2.6)		
RBC (x10^12/L)	4.6 (± 0.4)	4.9 (± 0.4)		
WBC (x10^9/L)	5.7 (± 1.6)	6.5 (± 2.3)		
neutrophils (x10^9/l)	3.3 (± 1.3)	4.0 (± 2.1)		
lymphocytes (x10^9/l)	1.4 (± 0.4)	1.5 (± 0.6)		
monocytes (x10^9/l)	0.6 (± 0.2)	0.7 (± 0.2)		
eosinophils (x10^9/l)	0.3 (± 0.2)	0.2 (± 0.1)		
basophils (x10^9/l)	0.04 (± 0.02)	0.05 (± 0.01)		
platelets (x10^9/l)	341.2 (± 55.2)	373.9 (± 75.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry values by visit

End point title	Blood chemistry values by visit
End point description: Absolute values are reported.	
End point type	Secondary
End point timeframe: At screening and at Visit 7	

End point values	Visit 7 population - ITT	Screening population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: units				
arithmetic mean (standard deviation)				
blood glucose (mg/dL)	83.7 (± 6.2)	86.6 (± 6.9)		
BUN (mmol/L)	4.3 (± 1.3)	4.40 (± 1.1)		
GOT/AST (U/L)	29.5 (± 9.3)	31.2 (± 10.5)		
GPT/ALT (U/L)	30.9 (± 20.6)	32.8 (± 18.6)		
alkaline phosphatase (U/L)	251.6 (± 85.9)	279.4 (± 104.1)		
total proteins (g/dL)	6.6 (± 0.4)	7.0 (± 0.4)		
albumin (g/dL)	4.0 (± 0.2)	4.30 (± 0.3)		
creatinine (mg/dL)	0.4 (± 0.1)	0.4 (± 0.1)		
bilirubin (mg/dL)	0.4 (± 0.3)	0.4 (± 0.2)		
serum iron (µg/dL)	66.2 (± 30.5)	82.9 (± 41.2)		
sodium (mmol/L)	141.4 (± 1.4)	142.3 (± 2.5)		
potassium (mmol/L)	4.5 (± 0.4)	4.7 (± 0.3)		
calcium (mmol/L)	2.4 (± 0.1)	2.5 (± 0.1)		
phosphorus (mg/dL)	5.1 (± 0.3)	5.1 (± 0.5)		
chloride (mol/L)	104.0 (± 1.8)	104.6 (± 2.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Urine analysis by visit

End point title	Urine analysis by visit
End point description: Absolute values are reported.	
End point type	Secondary
End point timeframe: at screening and at Visit 7	

End point values	Visit 7 population - ITT	Screening population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: units				
arithmetic mean (standard deviation)				
specific gravity	1022.4 (± 7.3)	1024.8 (± 5.9)		
pH	5.6 (± 0.7)	5.8 (± 0.6)		
glucose (mg/dL)	0.0 (± 0.0)	0.0 (± 0.0)		
protein (mg/dL)	6.8 (± 11.1)	11.5 (± 9.2)		
hemoglobin (mg/dL)	0.0 (± 0.0)	0.0 (± 0.0)		
ketones (mg/dL)	0.5 (± 2.1)	0.0 (± 0.0)		
bilirubin (mg/dL)	0.0 (± 0.0)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Special laboratory analysis by visit

End point title	Special laboratory analysis by visit
End point description: Absolute values are reported.	
End point type	Secondary
End point timeframe: at Visit 1 and at Visit 7	

End point values	Visit 1 (Baseline) population - ITT	Visit 7 population - ITT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: units				
arithmetic mean (standard deviation)				
total cholesterol (mmol/L)	4.3 (± 0.7)	4.3 (± 0.8)		
HDL cholesterol (mmol/L	1.2 (± 0.3)	1.3 (± 0.3)		
LDL cholesterol (mmol/L)	2.7 (± 0.6)	2.6 (± 0.7)		
HbA1c (%)	5.2 (± 0.3)	5.3 (± 0.3)		
CD4+ lymphocytes (count/mm3)	379.7 (± 152.0)	431.5 (± 147.2)		
a-fetoprotein (µg/L)	226.1 (± 161.8)	234.6 (± 180.7)		
blood cortisol (µg/dL)	15.9 (± 7.7)	13.8 (± 6.4)		
urinary cortisol (µg/24h)	39.9 (± 17.5)	29.4 (± 20.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At screening visit (day -30 --> 0), V1 (day 0), V2 (day 30), V3 (day 60), V4 (day 90), V5 (day 120), V6 (day 150), V7 (day 180).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	EryDex - Safety population

Reporting group description:

The safety population includes the 22 patients who have received at least one dose of planned trial treatment.

Serious adverse events	EryDex - Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4.5 %

Non-serious adverse events	EryDex - Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 22 (68.18%)		

Investigations Low serum iron levels subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
Vascular disorders Diastolic hypertension subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
General disorders and administration site conditions Fever subjects affected / exposed occurrences (all)	 3 / 22 (13.64%) 3		
Immune system disorders Low serum CD4+ lymphocytes levels subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 3 / 22 (13.64%) 3		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Otitis subjects affected / exposed occurrences (all) Urinary infection subjects affected / exposed occurrences (all) Herpes labialis subjects affected / exposed occurrences (all) Flu syndrome	 1 / 22 (4.55%) 1 2 / 22 (9.09%) 3 3 / 22 (13.64%) 4 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2		

subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3 1 / 22 (4.55%) 1		
Metabolism and nutrition disorders Hypercholesterolemia subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2011	During the study, there was an Amendment approved by the Ethic Committe of the Coordinating Centre on 11 July 2011. This amendment instituted the following procedure: only for the patients from the Department of Infantile Pediatrics and Neuro-Psychiatry - University La Sapienza, Rome, an additional 10 mL of blood was to be collected at the final visit (V7) to define the expression of mRNAs from several gene products, and to evaluate the cytokines and chemokines levels, the lymphocyte sub-populations and the RBC morphology, stability and biochemical properties.

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.

No limitations or caveats are applicable to this summary of results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24405665