



Clinical trial results:

Multicenter, randomized, double-blind, parallel-group study of intra-erythrocyte dexamethasone versus placebo in patients with steroid-dependent Crohn's disease

Summary

EudraCT number	2008-007329-38
Trial protocol	IT ES
Global end of trial date	30 December 2011

Results information

Result version number	v1 (current)
This version publication date	12 June 2022
First version publication date	12 June 2022

Trial information

Trial identification

Sponsor protocol code	CRODEX01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01277289
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 0236504470, info@erydel.com
Scientific contact	Clinical Trial Transparency Manager, Erydel S.p.A., +39 0236504470, 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	30 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2011
Global end of trial reached?	Yes
Global end of trial date	30 December 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Assessment of the efficacy of Ery-Dex vs placebo in maintaining patients with steroid-dependent Crohn's disease in clinical remission throughout 12 months without oral steroids.

Protection of trial subjects:

This study was conducted in accordance with the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice (GCP) and the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2009
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	Spain: 1
Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Romania: 1
Worldwide total number of subjects	51
EEA total number of subjects	51

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	44
From 65 to 84 years	7

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

There were 63 patients enrolled into the screening phase at 10 sites; of these, 51 patients (representing the Safety population) were randomized at 9 sites.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was a multicenter, randomized, double-blind, PLACEBO-controlled, parallel-group study comparing EryDex versus PLACEBO.

Arms

Are arms mutually exclusive?	Yes
Arm title	EryDex

Arm description:

EriDex (dexamethasone sodium phosphated administered as intra-erythrocyte drug at monthly intervals for 12 months).

Arm type	Experimental
Investigational medicinal product name	EriDex
Investigational medicinal product code	
Other name	dexamethasone sodium phosphate for encapsulation in human erythrocytes
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone sodium phosphate encapsulated in human erythrocytes (EryDex): vials of 250 mg / 10 ml

Monthly administration of EryDex (500 mg / 2 vials) for 12 administrations (12 months).

50 ml of "encapsulated" erythrocytes (previously taken from the same patient) after conditioning with Dexamethasone Sodium Phosphate (500 mg in 20 ml).

Arm title	Placebo comparator
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Arm description:

Placebo comparator (administered as intra-erythrocyte drug at monthly intervals for 12 months).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Monthly administration of Placebo for 12 administrations (12 months).

Placebo (10 ml NaCl, 0.372%).

Number of subjects in period 1	EryDex	Placebo comparator
Started	28	23
Completed	5	2
Not completed	23	21
Consent withdrawn by subject	1	1
Physician decision	1	-
Fragile vein	1	-
Adverse event, non-fatal	2	1
Violation	1	1
Premature closure of the study	4	2
Therapy failure and/or Crohn's surgery	13	16

Baseline characteristics

Reporting groups

Reporting group title	EryDex
Reporting group description: EriDex (dexamethasone sodium phosphated administered as intra-erythrocyte drug at monthly intervals for 12 months).	
Reporting group title	Placebo comparator
Reporting group description: Placebo comparator (administered as intra-erythrocyte drug at monthly intervals for 12 months).	

Reporting group values	EryDex	Placebo comparator	Total
Number of subjects	28	23	51
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	47.3	43.4	
standard deviation	± 14.9	± 12.5	-
Gender categorical Units: Subjects			
Female	20	7	27
Male	8	16	24

End points

End points reporting groups

Reporting group title	EryDex
Reporting group description: EriDex (dexamethasone sodium phosphated administered as intra-erythrocyte drug at monthly intervals for 12 months).	
Reporting group title	Placebo comparator
Reporting group description: Placebo comparator (administered as intra-erythrocyte drug at monthly intervals for 12 months).	

Primary: Proportion of patients maintaining steroid-free clinical remission (CDAI < 150) without surgery throughout 12 months

End point title	Proportion of patients maintaining steroid-free clinical remission (CDAI < 150) without surgery throughout 12 months ^[1]
End point description: The primary efficacy end-point is the proportion of patients maintaining steroid-free clinical remission (CDAI < 150) without surgery. The number of patients completing the 12 months of the study was low (n=51); therefore, only a descriptive analysis was performed. No statistical analyses were performed for the secondary end-points because of the early study termination.	
End point type	Primary
End point timeframe: 12 months since the day of the first 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: The number of patients completing the 12 months of the study was low (n=51); therefore, only a descriptive analysis was performed.

End point values	EryDex	Placebo comparator		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	23		
Units: percentage				
number (not applicable)	17.9	8.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At days 15, 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 360 (follow up), 420 (follow up) and 600 (follow up).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	12

Reporting groups

Reporting group title	EriDex - Safety set
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Reporting group description: -

Reporting group title	Placebo - Safety set
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Reporting group description: -

Serious adverse events	EriDex - Safety set	Placebo - Safety set	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 28 (21.43%)	4 / 23 (17.39%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 28 (7.14%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 28 (3.57%)	3 / 23 (13.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1.5 %

Non-serious adverse events	EriDex - Safety set	Placebo - Safety set	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 28 (60.71%)	15 / 23 (65.22%)	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 28 (21.43%)	4 / 23 (17.39%)	
occurrences (all)	7	5	
Hyperpyrexia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Irritability			
subjects affected / exposed	5 / 28 (17.86%)	2 / 23 (8.70%)	
occurrences (all)	6	2	
Oedema			
subjects affected / exposed	3 / 28 (10.71%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal			

disorders			
Influenza			
subjects affected / exposed	4 / 28 (14.29%)	4 / 23 (17.39%)	
occurrences (all)	4	7	
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Psychiatric disorders			
Affect lability			
subjects affected / exposed	3 / 28 (10.71%)	1 / 23 (4.35%)	
occurrences (all)	3	1	
Insomnia			
subjects affected / exposed	4 / 28 (14.29%)	3 / 23 (13.04%)	
occurrences (all)	5	3	
Investigations			
Blood iron decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Haematocrit decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Red blood cell count decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	3 / 28 (10.71%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Limb injury			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 23 (13.04%) 12	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 23 (0.00%) 0	
Anaemia macrocytic subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	3 / 23 (13.04%) 3	
Leukocytosis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 2	0 / 23 (0.00%) 0	
Neutrophilia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 2	0 / 23 (0.00%) 0	
Eye disorders Ocular hypertension subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 3	1 / 23 (4.35%) 1	
Acetonaemic vomiting subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	1 / 23 (4.35%) 1	
Anal fistula subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Crohn's disease			

subjects affected / exposed	2 / 28 (7.14%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Dyspepsia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Faecal incontinence			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Faeces discoloured			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal reflux disease			
subjects affected / exposed	0 / 28 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	10	
Haematochezia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Intestinal obstruction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	3 / 28 (10.71%)	2 / 23 (8.70%)	
occurrences (all)	3	2	
Rectal tenesmus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Subileus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			

Dermatitis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Rash subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Skin striae subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	1 / 23 (4.35%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Pollakiuria subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 23 (0.00%) 0	
Renal colic subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5	0 / 23 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	2 / 23 (8.70%) 2	
Back pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	1 / 23 (4.35%) 1	

Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Infections and infestations			
Ear infection subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Herpes zoster ophthalmicus subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Oral herpes subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	
Tonsillitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 23 (4.35%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2008	- change of exclusion criteria re: hemoglobin (Hb < 8 gr/dl, instead of Hb < 10 gr/dl) and liver enzymes (AST [GOT] ≥3x ULN and alkaline phosphatase ≥3x ULN, instead of ≥5x ULN for both parameters) - washout from previous immunosuppressants reduced from 6 to 4 months - the exclusion of subjects with prior therapy based on anti-TNF within 3 months of the enrolment was specified - the "Clostridium difficile" stool test was introduced at baseline - antibiotics were permitted only if necessary because of infections and for not longer than 15 days. The use of antibiotics as specific therapy for Crohn's Disease was not allowed - follow-up prolonged up to 6 months to check eventual relapse of disease in patients completing the study - patient's diary completion extended from 7 days to the entire month between treatments - SF 36 questionnaire on quality of life was added - ICF was updated accordingly - an additional ICF was introduced to collect long-term health-related information, in particular relapses, in patients withdrawing the consent to the general study
20 July 2009	- additional samples were requested for dexamethasone dosing in infusion bags from visit 4 to visit 11 to check stable dosing and correct encapsulation procedures in the long term; blood would be taken directly from the infusion bag; no additional venipuncture needed - definition of resistance to AZT/6-MP/MTX corrected, because of a typing error, to stay in line with international guidelines (inability to suspend steroids after at least 4 months of AZT/6-MP/MTX treatment at appropriate dosage; instead of 6 months) - other typing errors were corrected - specifications added in the labeling of tubes for the plasma dexamethasone concentrations - ICF was updated accordingly
22 June 2010	- change in the screening and identification of patients suitable for study (without changing the target patient population): allowed inclusion of subjects with at least one episode of relapse (CDAI > 150) in the last 12 months, in clinical remission (CDAI < 150) for at least four weeks, and on stable therapy with at least 10 mg of methylprednisolone (or equivalent) for at least 2 weeks - ICF was updated accordingly - reference to the already approved change of the Coordinating Investigator - change in the name of the CRO following the study - change in the number of participating sites (up to 15 in total) - end of patients' enrolment: extended to December 2011 - minor, non substantial, changes to provide clarifications on issues that emerged and were discussed during the course of the study, without changes in the study conduct

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: