Ensayo fase III

IEDAT

A Multi-center, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Effects of ***I***ntra-***E***rythrocyte ***D***examethasone Sodium Phosphate on Neurological Symptoms in Patients with ***A***taxia ***T***elangiectasia

Los corticoides por via oral son útiles en la Ataxia Telangiectasia, pero con efectos adversos

Potential Therapeutic Strategies: Oral bethamethasone


OBSERVATION

Betamethasone and Improvement of Neurological Symptoms in Ataxia-Telangiectasia


Steroid-induced improvement of neurological signs in ataxia-telangiectasia patients


Efficacy of very-low-dose betamethasone on neurological symptoms in ataxia-telangiectasia


In ataxia-telangiectasia betamethasone response is inversely correlated to cerebellar atrophy and directly to antioxidative capacity

- Serendipitous findings have suggested beneficial effects of corticosteroids in the treatment of AT
- Short term trials with an oral corticosteroid showed improvement of neurological symptoms in AT patients
- Significant steroid side effects led to discontinuation of treatment and search for other options

Corticoides (dexametasona) intraeritrocitarios . Ensayo fase II

IEDAT Phase II trial

Chessa *et al. Orphanet Journal of Rare Diseases* 2014, 9:5
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ORPHANET JOURNAL OF RARE DISEASES

RESEARCH Open Access

Intra-Erythrocyte Infusion of Dexamethasone Reduces Neurological Symptoms in Ataxia Teleangiectasia Patients: Results of a Phase 2 Trial

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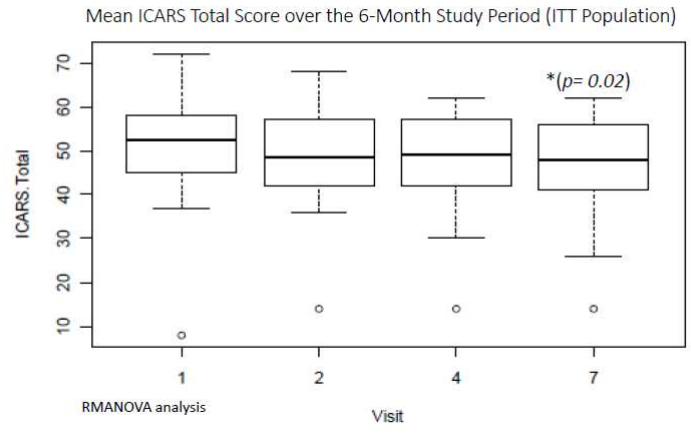
Corticoides (dexametasona) intraeritrocitarios . Ensayo fase II
Mejora escala de ataxia (ICARS)

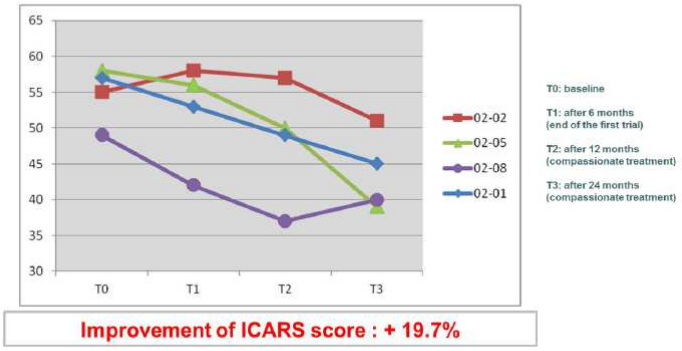
Primary efficacy end-point met



Corticoides (dexametasona) intraeritrocitarios . Seguimiento a largo plazo tras el Ensayo fase II Mejora escala de ataxia (ICARS)

Chronic treatment with EDS

Long term benefit confirmed with compassionate treatment up to 2 years



Improvement of ICARS score : + 19.7%

At the end of the first 6-month trial, 4 male subjects (mean age 10,6 years) continued EDS treatment for an adjunctive 24-month period

Seguridad Dexametasona en eritrocitos

En diversos estudios se han tratado en total:

- 209 sujetos, con 1827 infusiones en total.
- 51 son pediátricos (< 18 años): Fibrosis quistica 11, Enf Crohn 19, A-T 22)

Sin toxicidad relacionada con el procedimiento ni con la dexametasona.

Algunos han sido tratados largo tiempo, hasta 36 meses

Ensayo fase III

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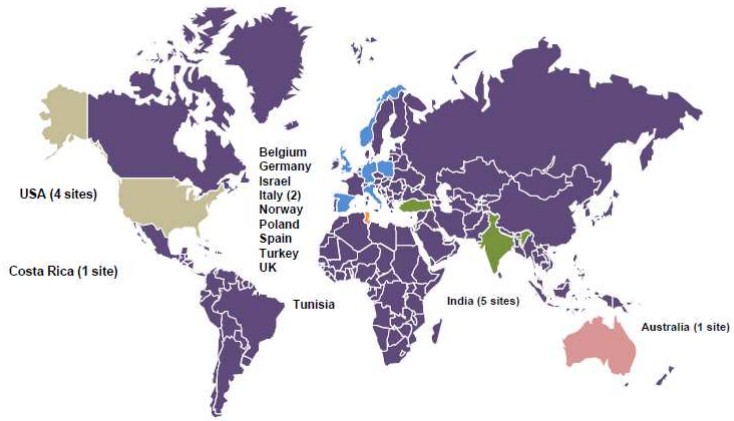
Ensayo fase III
Centros participantes

GEOGRAPHIC DISTRIBUTION



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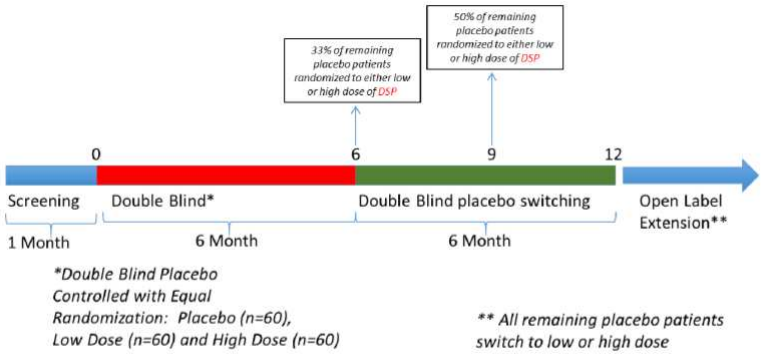
Esquema

Scheme of Pivotal Trial in AT



**Double Blind Placebo Controlled with Equal Randomization: Placebo (n=60), Low Dose (n=60) and High Dose (n=60)*

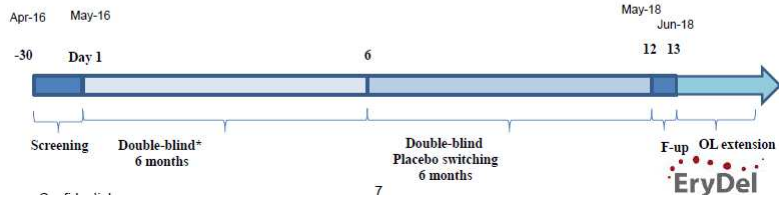
*** All remaining placebo patients switch to low or high dose*

Schedule of Visits and Assessments: 6-Month Initial Treatment Period

Visit (V) #	Screening	V1		V2	V3	V4	V5	V6		V7	V8	V9
Study Day or Month (D/M) #	D -30 to -1	D0/1		D2	D15	M1	M2	M3		M4	M5	M6 (a,b)
Procedure		Pre(c)	Post(c)					Pre(c)	Post(c)			
Informed Consent Signature	X											
Medical History	X											
Inclusion/Exclusion Criteria (v)	X	X										
EDS-EP Infusion (h)		1				2	3	4		5	6	
Neurological Examination	X	X						X				X
Physical Examination	X	X	X			X	X	X	X	X	X	X
Vital Signs	X	X	X			X	X	X	X	X	X	X
ECG	X	X(d)						X				X
Routine Laboratory Tests (e)	X	X(d)						X				X
Bone Mineral Density		X										X
Serum Pregnancy Test (o)	X	X										X
ICARS (with video recording)	X(n)	X(n)						X				X
CGI-C								X				X
CGI-S	X	X						X				X
VABS		X						X				X
A-TNEST		X						X				X
Quality of Life (EQ-5D-Y)		X						X				X
C-SSRS		X										X
RBC osmotic resistance (t)	X	X						X				
Special Laboratory Tests	X(f)	X(f,g)	X(m)	X(m)	X(m)	X(m)						X(f,g)
Hemolysis Panel (s)		X	X	X	X			X	X			
Urinary Cortisol	X	X	X	X	X	X		X				X
Genetic AT diagnosis (q)	X											
Mini-ATM detection		X				X						X
Dexamethasone PK sample		X(i)	X(i)	X(j)	X(k)	X(l)	X(l)	X(l)	X(l)	X(l)	X(l)	X(l)
EDS end product sample		X				X	X	X		X	X	
Prior/Concomitant Treatments	Throughout the duration of the study											
Adverse Events	Throughout the duration of the study											

Projected Timelines

	Start Date	End Date
Study Start-Up	Ongoing	
Enrolment (12 months expected)	Apr-16	Apr-17
Treatment (Last Day 1 to Last Month 12)	May-17	May-18
Last Month 6 visit		Nov-17
Follow-Up Period (last Month 13)	May-18	Jun-18
Final Lock Data	Jun-18	Jul-18
Final Stats Analysis	Jul-18	Aug-18
Final Clinical Study Report	Aug-18	Oct-18



Ensayo fase III
Medidas de eficacia

Ensayo fase III
Medidas de eficacia

- **Escala de ataxia (ICARS),**
- **escala de mejora global (CGI-S y CGI-C) ,**
- **escala adaptación personal y social (VABS) y**
- **escala de calidad de vida (EQ-5D-Y)**