Clinical trial results: *Full title of Trial**

Summary

An open-label, prospective, multicentric pilot study evaluating safety and symptomatics effects of low dose Naltrexone in patients with primary progressive multiple sclerosis.

EudraCT number*	
Trial protocol	safety protocol
Global end of trial date*	MARCH 2007

Trial information

Trial identification

additional study identifier

Sponsor protocol code*	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	if available
WHO universal trial number (UTN)	-

Notes:

Sponsors details*

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	
Scientific contact	

Notes:

Paediatric regulatory details*

Is trial part of an agreed paediatricinvestigation plan (PIP)	NO
Does article 45 of REGULATION (EC) No1901/2006 apply to this trial?	NO
Does article 46 of REGULATION (EC) No1901/2006 apply to this trial?	NO

Results analysis stage

Analysis stage*	FINAL
Date of interim/final analysis*	evauation of BE at January 2008
Is this the analysis of the primary completion data?*	Yes

Global end of trial reached?*	Yes
Global end of trial date*	january 2008
Was the trial ended prematurely?	no

General information about the trial

Main objective of the trial*: *Enter a description for the mail objective(s) of the trial*

Actual start date of recruitment*	December 2006
Long term follow-up planned*	no
If Yes, rationale:	Safety Efficacy Ethical reason Regulatory reason Scientific research
Duration	december 2006-january 2008
Independent data monitoring committee(IDMC) involvement?*	no
Protection of trial subjects*:	Insurance
Background therapy:	
Evidence for comparator:	

Population of trial subjects

Subjects enrolled per country

Country:	italy
Planned number of subjects	40
Actual Number of subjects enrolled*	40
Worldwide total number of subjects	40
EEA total number of subjects	

Subjects enrolled per age group

In utero*	no
Preterm newborn - gestational age < 37wks*	no
Newborns (0-27 days)*	no
Infants and toddlers (28 days-23months)*	no
Children (2-11 years)*	no
Adolescents (12-17 years)*	no
Adults (18-64 years)*	yes
From 65 to 84 years*	yes
85 years and over*	no

Subject disposition

Recruitment details: *Enter key information relevant to the recruitment process for the trial (eg gates of recruitment period and territories)*

Pre-assignment - *Screening details*: *Enter relevant information related to screening (eg screening criteria, significant events and approaches)*

Period 1

Period title*	*overall trial*
Is this the baseline period?	no
Allocation method*	non-randomimsed
Blinding used*	Not blinded

Arms

Arm title*	A pilot trial of low-dose naltrexone in primary progressive multiple sclerosis
Arm description:	
Arm type*	experimental
Investigational medicinal product name*	**NALTREXONE**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**pills**
Routes of administration*	**oral**
Dosage and administration details*	4 mg

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	december 2006	
Completed*	march 2007	
Subject non-completion reason (if applicable)		
AE, non fatal	(40)	urinary infection, enuresis, disease worsening, >2 fold increase of bilirubin
AE, fatal	NO	
Consent withdrawn by subject		
Lack of efficacy		
Lost to follow up		
Physician decision		
Pregnancy		
Protocol Deviation	1	protocol violation(opioid drug use)

Other		

Baseline characteristics

Reporting groups* Overall cohort

Reporting group title*	LDN treated patient
Number of subjects at the baseline*	40

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	*Safety*
Subject analysis set type*	Safety analysis
Subject analysis set description*	*evaluate safety of low dose naltrexone in PPSMpts*
Number of subjects in subjects analysis set*	*35*

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical	??	??	??

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	18–65 years aged mean age: 53.4	Years Months Weeks Days	Arithmetic Mean Median least square mean geometric mean log mean	full range (min-max) standard deviation inter quartile range

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	female:male =21:19		Female Male

Study specific characteristics

	Characteristic title*	Units*	Categories*	Number of subject for each categories

Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				

End points

Add subject analysis set if you wish to report on groups different form reporting groups defined above

Subject analysis set title*	safety analysis
Subject analysis set type*	**primary outcome:** Safety analyses :vital signs, adverse event monitoring, and complete biochemical tests [including blood cell count, liver and kidney function, electrolytes, plasma glucose, cholesterol, eritro-sedimentation rate (ESR), and urinary analysis]
Subject analysis set description*	**Secondary outcome clinical scales** : Visual Analogue Scale, Modified Ashworth Scale, Fatigue Severity Scale, Beck Depression Inventory and blood, urinary measures
Number of subject in subject analysis set *	intention-to-treat analysis:40

End points definitions

End point title*		
		Values
Countable or measurable?*		-
If countable, Countable units*:		
If measurable, Measurable units*		
Measure type*:		
Precision/dyspersion type*		

End point type*	SAFETY evaluation : vital signs, adverse event monitoring, and complete biochemical tests

End point timeframe*:

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*			
Period	6 months		
Arms	1		
subject analysis sets	40		

Adverse events

Adverse events information

Timeframe for reporting adverse events*: *Enter the time point(s) or time period for AE assessment*

First patient first visit:
Last recruitment date:
Study closure:

Adverse event reporting additional description: *Enter information about the AE collection and provide details about the method of assessment and monitoring*

Major (grade III or IV) Lung carcinoma and renal failure Total 2 (5%)
Minor (grade I or II) Irritability 5 (12.5%)
Hematological abnormalities 14 (35%)
Urinary infection 8 (20%)
Other 8 (20%)

Assessment type*	Systematic or Non Systematic
Frequency threshold for reporting non-serious adverse events*	**Lung carcinoma and renal failure Total 2 (5%)** **Irritability 5 (12.5%)** **Hematological abnormalities 14 (35%)** **Urinary infection 8 (20%)** **Other 8 (20%)**

Dictionary used

Dictionary name*	MedDRA or CTCAE
Dictionary version*	

Adverse events reporting group definition

Use arms from baseline period as reporting groups
OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	40
Subjects affected by non -SAE*	27/40
Total number of deaths (all causes)*	no
Total number of deaths resulting from adverse event*	no

Serious adverse event details and values

System organ class*:

Event term*:

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number

Non - Serious adverse event details and values

System organ class*:

Event term*:

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? Yes or No

Date	**Amendment**

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? **Y e s** o r No : **4 drops out**

If Yes, Interruption date

Interruption descrption

One patient (ID_1) decided to interrupt the treatment 48 days after the beginning due to the occurrence of enuresis. ID_13 decided to interrupt the treatment 5 months after the beginning due to a subacute clinical worsening of left upper and lower limb hypostenia. Neurological worsening was not confirmed 1 month after treatment discontinuation. ID_16 exited the study 3 months after the beginning of the treatment because of a >2 fold increase of bilirubin (total 2.32; indirect 1.46). ID_38 exited the study 4 months after

the beginning of treatment because of a urinary infection causing renal failure (creatinine 3.9 mg/dL) not requiring dialysis. ID_40 dropped out for a major protocol violation: 15 days after the beginning of the study, the patient admitted the use of an opioid-containing drug (tramadol) to treat pain.

Limitations and caveats

None reported

Online references

Enter PubMed identifier (PMID)

PMID: .....

A pilot trial of low-dose naltrexone in primary progressive multiple sclerosis

M Gironi, F Martinelli-Boneschi, P Sacerdote, C Solaro, M Zaffaroni, R Cavarretta, L Moiola, S Bucello, M Radaelli, V
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