Clinical trial results:
Immune tolerance induction in MS patients with neutralizing antibodies against interferon-beta

Summary

EudraCT number	2009-013284-19
Trial protocol	AT
Global end of trial date	30 September 2010

Results information

Result version number	v1 (current)
This version publication date	21 October 2020
First version publication date	21 October 2020

Trial information

Trial identification

Sponsor protocol code	HINABS-ITI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Christoph-Probst-Platz 1, Innrain 52 A, Innsbruck, Austria, 6020
Public contact	Priv.Doz. Dr. Harald Hegen, Medical University Innsbruck, University Hospital for Neurology, +43 (0)512- 504- 24279, harald.hegen@tirol-kliniken.at
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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 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2010
Global end of trial reached?	Yes
Global end of trial date	30 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

How many multiple slerosis patients show a reduction of the neutralizing antibodies < 100 neutralizing units after 3 months of weekly intravenous interferon-beta infusion.

Protection of trial subjects:

To reduce side effects such as flu-like symptoms (FLS), 1000 mg paracetamol were administered intravenously prior to each IFNβ infusion.

Background therapy:

All subjets received IFNβ before enrolled in the trial.

Evidence for comparator:

No comparators were tested in this trial.

Actual start date of recruitment	10 December 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	Austria: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were eligible if they were diagnosed as relapsing MS or clinically isolated syndrome (CIS) according to the revised McDonalds criteria 2005, received previous treatment with any IFNβ preparation and were NAb positive with a titer >500 TRU (10-fold reduction unit) at screening.

Pre-assignment

Screening details:

Previous IFNβ treatment had to be interrupted for at least 7 days before baseline visit. Patients, who did not show sufficient MxA gene expression after administration of the study dose of 1500µg IFNβ-1b at baseline or at week 1, were withdrawn from the study.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IFNβ-1b treatment

Arm description:

We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression

Arm type	Experimental
Investigational medicinal product name	Interferon Beta-1b
Investigational medicinal product code	
Other name	Betaferon
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 1500µg IFNβ-1b reconstituted in 100 ml 0.9% NaCl intravenously once a week over 3 months (i.e. a total of 13 infusions).

Number of subjects in period 1	IFNβ-1b treatment
Started	10
Completed	9
Not completed	1
Lacking MxA induction	1

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IFNβ-1b follow-up

Arm description:

We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression

Arm type	Experimental
Investigational medicinal product name	Interferon Beta-1b
Investigational medicinal product code	
Other name	Betaferon
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 1500µg IFNβ-1b reconstituted in 100 ml 0.9% NaCl intravenously once a week over 3 months (i.e. a total of 13 infusions).

Number of subjects in period 2	IFNβ-1b follow-up
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	IFNβ-1b treatment
Reporting group description:	
We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression	

Reporting group values	IFNβ-1b treatment	Total	
Number of subjects	10	10	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	10	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	47.4		
standard deviation	± 10.019	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	5	5	

End points

End points reporting groups

Reporting group title	IFNβ-1b treatment
Reporting group description:	
We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression	
Reporting group title	IFNβ-1b follow-up
Reporting group description:	
We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression	

Primary: NAb titer

End point title	NAb titer
End point description:	
Blood collections were performed at screening, then monthly at baseline, week 4, 8 and 12, as well as at follow-up after 24 weeks. At baseline and weeks 4, 8 and12 blood samples were withdrawn immediately before and 4h after IFNβ administration.	
End point type	Primary
End point timeframe:	
Day 0 (baseline)- week 24	

End point values	IFNβ-1b treatment	IFNβ-1b follow-up		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: TRU				
median (inter-quartile range (Q1-Q3))	1429 (902 to 2995)	2175 (1803 to 2519)		

Statistical analyses

Statistical analysis title	NAb titers
Statistical analysis description:	
Median NAb titer at follow-up was not significantly different compared to baseline.	
Comparison groups	IFNβ-1b treatment v IFNβ-1b follow-up
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Week 0- week 24	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	IFNβ-1b treatment and follow-up

Reporting group description:

We aimed to investigate whether the repeated high-dose intravenous IFNβ administration in patients with high NAb titers leads to a sustained reversion of NAbs and an increase of MxA expression

Serious adverse events	IFNβ-1b treatment and follow-up		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	IFNβ-1b treatment and follow-up		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)		
Cardiac disorders			
Hypotonia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Immune system disorders			
Relapse			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Flu-like symptoms			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Infections and infestations Respiratory tract infection subjects affected / exposed occurrences (all)	 2 / 10 (20.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25878009