Clinical trial results:
A prospective, multicentre, open label, exploratory study to investigate the ability of the Heidelberg Assay Panel and the B-Cell /Antibody response panel to predict the clinical effect of Octagam 5% in subjects with relapsing/remitting (RR) multiple sclerosis (MS).

Summary

EudraCT number	2008-004579-22
Trial protocol	AT DE
Global end of trial date	21 December 2010

Results information

Result version number	v1 (current)
This version publication date	31 December 2016
First version publication date	31 December 2016

Trial information

Trial identification

Sponsor protocol code	GAM-25

Additional study identifiers

ISRCTN number	ISRCTN57377482
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma AG
Sponsor organisation address	Seidenstrasse 2, Lachen, Switzerland, CH-8853
Public contact	Clinical Research Department, Octapharma Pharmazeutika Prod.Ges.m.b.H, 0043 161032-0,
Scientific contact	Clinical Research Department, Octapharma Pharmazeutika Prod.Ges.m.b.H, 0043 161032-0,

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	28 August 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

No primary objective has been chosen, as the study was an exploratory study to identify biomarkers that could be predictive for the clinical response to IVIG treatment in patients with RR-MS.
Objective was to investigate :
-whether any parameters of the HAP correlate with the clinical effect observed following Octagam 5% treatment in subjects with relapsing-remitting MS and whether any B-cell/antibody responses correlate with the clinical effect observed following Octagam 5% treatment in subjects with RR MS.
- the proportion of subjects responding to Octagam 5% treatment vs. subjects not responding and the relapse activity during the observation period.
- efficacy as assessed by neurological examinations using the Expanded Disability Status Scale (EDSS) and Functional System (FS) and the Multiple Sclerosis Functional Composite measure (MSFC).
- the change of T2/T1 lesion load and active lesions as demonstrated by contrast enhancement on (MRI)
-tolerability of Octagam 5%

Protection of trial subjects:

This trial was conducted in accordance to the principles of GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product. Throughout the study safety was assessed, such as occurrence of AEs, safety labs, vital signs and physical/neurological examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 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: 13
Country: Number of subjects enrolled	Germany: 20
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	33
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with RR-MS with an EDSS between 0 and 3.5 (0 to 3.5) for whom first-line disease-modifying treatments were either contraindicated or not tolerated and who did not have any contraindications for IVIG therapy were eligible to take part in the study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Octagam 5%

Arm description:

Open-label arm of RR-MS patients who had to be treated with 0.4 g/kg Octagam 5% for 20 infusions in 4-week (+/- 1 week) intervals.

Arm type	Experimental
Investigational medicinal product name	Octagam 5%, Human normal immunoglobulin 5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A total of 20 intravenous infusions of 0.4 g/kg in 4-week (±1 week) intervals per patient

Number of subjects in period 1	Octagam 5%
Started	33
Completed	0
Not completed	33
early termination of the study	33

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	33	33	
Age categorical Units: Subjects			
Adults (18-64 years)	33	33	
Age continuous Units: years			
arithmetic mean	35.55		
standard deviation	± 10.41	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	10	10	

End points

End points reporting groups

Reporting group title	Octagam 5%

Reporting group description:

Open-label arm of RR-MS patients who had to be treated with 0.4 g/kg Octagam 5% for 20 infusions in 4-week (+/- 1 week) intervals.

Primary: No primary objective as the study was an exploratory study

End point title	No primary objective as the study was an exploratory study[1]

End point description:

No primary objective has been chosen, as the study was an exploratory study to identify biomarkers that could be predictive for the clinical response to IVIG treatment in patients with RR-MS.
All data collected were summarised by means of descriptive statistics to be understood in the exploratory sense; no confirmatory hypothesis testing was planned. Due to the exploratory nature of the study no sample size calculation was done.

Because of the early termination of the study due to safety concerns that arose from post-marketing data, none of the patients, except one completed the study with all Octagam 5% infusions as planned.

End point type	Primary

End point timeframe:

total study

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: All data collected were summarised by means of descriptive statistics to be understood in the exploratory sense; no confirmatory hypothesis testing was planned. Due to the exploratory nature of the study no sample size calculation was done.

End point values	Octagam 5%			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: none				

Notes:

[2] - study exloratory only, analyses not applicable

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the study, patients were monitored for AEs.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0
Reporting groups	
Reporting group title	Octagam 5%
Reporting group description: AEs in more that 1 patient	

Serious adverse events	Octagam 5%		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Octagam 5%		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 33 (69.70%)		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 33 (24.24%)		
occurrences (all)	15		
Migraine			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Ear and labyrinth disorders			

Vertigo subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 5 2 / 33 (6.06%) 3		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	8 / 33 (24.24%) 12 4 / 33 (12.12%) 4 3 / 33 (9.09%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2009	Amendment 1 (main changes): According to results of further pre-study investigations, it was decided to delete some of the originally described HAP parameters. It was not clearly differentiated between stimulation and ex vivo incubation of blood samples. It mentioned "IVIG" for incubation of blood samples. The wording was specified. "IVIG" was replaced by "Octagam 5%". Laboratory methods to determine the parameters were amended. Serum parameters were defined as BARP endpoint and EDTA blood samples were to be tested only from patients of the Innsbruck study site. An increase of the EDSS of at least 1 step was defined as non-response within this study. It was agreed that a continuous increase of EDSS of at least 2 steps without an underlying relapse had to be considered as a switch of the disease to the secondary progressive form and that those patients had to be withdrawn from the study.
26 August 2009	Amendment 2 (main changes): The time frame for baseline investigations was extended from 1 week to 2 weeks. Bicarbonate was deleted from the clinical chemistry parameters to be assessed. The duration of the study was prolonged from 18 to 24 months. In accordance with new Octapharma drug safety Standard Operating Procedures (SOPs), a few updates were made to the protocol safety section.
23 November 2009	Amendment 3 (main changes): The study was prolonged from 48 weeks to 80 weeks to increase the diagnostic value of the study markedly and to enhance the chances to differentiate clinical responders from non-responders.
27 September 2010	Amendment 4 (main changes): The study duration was prolonged to 1st quarter of 2012. Exclusion criterion No. 16 was clarified: Participation in another clinical study involving an IMP was not allowed. However, studies comprising data or blood sampling collections on a regular or long-term basis are exempt from this exclusion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 October 2010	Because of the early termination of the study due to safety concerns that arose from post-marketing data, none of the patients, except one completed the study with all Octagam 5% infusions as planned. This limited the evaluation of the data. No annual relapse rate could be described.	-

Notes:

Limitations and caveats

None reported