Clinical trial results:
ROLE OF ENDOTHELIAL INFLAMMATION IN DEMYELINATING DISEASES OF THE CENTRAL NERVOUS SYSTEM

Summary

EudraCT number	2014-000254-11
Trial protocol	DK
Global end of trial date	15 August 2018

Results information

Result version number	v1 (current)
This version publication date	07 April 2021
First version publication date	07 April 2021
Summary attachment (see zip file)	Article (NFL DMF.pdf)

Trial information

Trial identification

Sponsor protocol code	33375

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J.B. Winslows vej 4, Odense C, Denmark, 5000
Public contact	MS clinic, prof Illes, Department of Neurology, zsolt.illes@rsyd.dk
Scientific contact	MS clinic, prof Illes, Department of Neurology, 0045 53379541, zsolt.illes@rsyd.dk

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 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 August 2018
Global end of trial reached?	Yes
Global end of trial date	15 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Screening for a prognostic biomarker regarding MS

Protection of trial subjects:

We followed international and national guidelines, when collecting blood and CSF.

Background therapy:

None

Evidence for comparator:

No comparators

Actual start date of recruitment	30 April 2014
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	Denmark: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	104
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

April 2014 until August 2016, untreated newly diagnosed patients with multiple sclerosis

Pre-assignment

Screening details:

To be eligible to participate in this study, candidates must meet the following eligibility criteria at the Screening/Baseline Visit:
Patients with relapsing remitting multiple sclerosis (RRMS) fulfilling the McDonald criteria.
Treatment-naïve patients and patients treated with first-line disease modifying treatment (DMTs);
Age 18-60

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Baseline

Arm description:

pretreatment

Arm type	untreated

No investigational medicinal product assigned in this arm

Arm title	1-year treatment

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	dimethyl fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

240 mg twice a day

Number of subjects in period 1	Baseline	1-year treatment
Started	52	52
Completed	52	52

Baseline characteristics

Reporting groups	
Reporting group title	Baseline
Reporting group description: pretreatment	
Reporting group title	1-year treatment
Reporting group description: -	

Reporting group values	Baseline	1-year treatment	Total
Number of subjects	52	52	104
Age categorical			
Newly diagnosed untreated patients with multiple sclerosis			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	52	52	104
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
geometric mean	34.1	34.1	
standard deviation	± 8.7	± 8.7	-
Gender categorical			
Units: Subjects			
Female	45	45	90
Male	7	7	14

Subject analysis sets	
Subject analysis set title	Patients
Subject analysis set type	Full analysis

Subject analysis set description:

We included untreated (naïve) newly diagnosed MS patients with RRMS according to the McDonald 2010 criteria. All patients had oligoclonal bands (OCBs) in the CSF (n=52).

Reporting group values	Patients		
Number of subjects	52		
Age categorical			
Newly diagnosed untreated patients with multiple sclerosis			
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)	52		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
geometric mean	34.1		
standard deviation	± 8.7		
Gender categorical			
Units: Subjects			
Female	45		
Male	7		

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description: pretreatment	
Reporting group title	1-year treatment
Reporting group description: -	
Subject analysis set title	Patients
Subject analysis set type	Full analysis

Subject analysis set description:

We included untreated (naïve) newly diagnosed MS patients with RRMS according to the McDonald 2010 criteria. All patients had oligoclonal bands (OCBs) in the CSF (n=52).

Primary: neurofilament light chain

End point title	neurofilament light chain

End point description:

End point type	Primary

End point timeframe:

1 year

End point values	Baseline	1-year treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: pg/mL				
geometric mean (standard deviation)	2368 (± 1947)	604 (± 472)		

Statistical analyses

Statistical analysis title	Statistics

Statistical analysis description:

We described baseline characteristics with means and SDs for continuous variables and percentages for binary variables.
Linear fit regression was performed using Spearman linear fit regression to calculate coefficients and linearity between NFL in CSF, plasma and serum. Data was checked for normality using D'Agostino & Pearson normality test.
Receiver operating characteristic (ROC) analysis was performed to identify cut-offs of NFL concentration in blood and CSF that differentiate health

Comparison groups	Baseline v 1-year treatment

Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Regression, Linear

Notes:

[1] - comparing to the pre-treatment period

Adverse events

Adverse events information	
Timeframe for reporting adverse events: April 30 2014 till august 14 2018	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1
Reporting groups	
Reporting group title	Adverse Events

Reporting group description: -

Serious adverse events	Adverse Events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (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	Adverse Events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 52 (96.15%)		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Gastrointestinal disorders			
Gastrointestinal			
subjects affected / exposed	25 / 52 (48.08%)		
occurrences (all)	25		
Skin and subcutaneous tissue disorders			
Flushing			
subjects affected / exposed	30 / 52 (57.69%)		
occurrences (all)	30		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Results are published in Journal of Neurology, Neurosurgery and Psychiatry attached

Notes: