



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 (\pm 1947) | 604 (\pm 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

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|-----------------|--------|
| 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.

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