



Clinical trial results:

TMP001 in relapsing-remitting multiple sclerosis: a multicentre open, baseline-controlled phase IIa clinical trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-004483-38 |
| Trial protocol | DE |
| Global end of trial date | 20 April 2018 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 June 2022 |
| First version publication date | 13 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | TMP001_MS |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Fraunhofer Gesellschaft for its Institute Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) - now ITMP |
| Sponsor organisation address | Theodor-Stern-Kai 7, Frankfurt, Germany, 60596 |
| Public contact | Project group TMP, Fraunhofer IME, Clinical Research, 0049 69630180208, clinical.research@ime.fraunhofer.de |
| Scientific contact | Project group TMP, Fraunhofer IME, Clinical Research, 0049 69630180208, clinical.research@ime.fraunhofer.de |

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 | 14 April 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 April 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Average total number of contrast enhancing lesions (CELs) on brain MRI scans at weeks 12, 16, 20, and 24 compared to the average total number of CELs on brain MRI scans at week -4 and baseline (BL).

Protection of trial subjects:

Subjects were included after assessing adherence to inclusion and exclusion criteria. Safety lab was performed at each study visit: Haematology, blood chemistry, coagulation and urinalysis were done every 4 weeks, intracellular cytokine profiles were measured and incidence and severity of AEs assessed and documented

Background therapy:

patients with relapses may be treated, e.g. with intravenous

In case of relapses methylprednisolone 1000 mg per day for 3 to 5 days was allowed.

The following concomitant medications were also allowed:

- 4-aminopyridine if used per label and maintained on a stable regimen for at least 30 days prior to inclusion and throughout the study.
- Medications used to treat MS symptoms such as spasticity, bladder impairment, pain, or depression.
- Short courses of high-dose corticosteroids per local standard of care in the treatment of protocol-defined relapse of MS disease.
- Corticosteroids that are administered by non-systemic routes (e.g., topical, inhaled)

Evidence for comparator:

no comparator

| | |
|---|--------------|
| Actual start date of recruitment | 01 June 2015 |
| 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 | Germany: 4 |
| Worldwide total number of subjects | 4 |
| EEA total number of subjects | 4 |

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) | 4 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patient with relapsing remitting Multiple Sclerosis (RRMS) were screened for eligibility and included in the study. Recruitment started 14.04.2016

Pre-assignment

Screening details:

Patients fulfilling inclusion criteria had a run-in phase for 28 days. Definite diagnosis of RRMS, at least 1 documented relapse during the previous year OR at least 2 documented relapses during the previous 2 years, at least one contrast-enhancing lesion (CEL) on screening MRI

Period 1

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

Blinding implementation details:

No blinding required since all patient received study treatment in a baseline-controlled design

Arms

| | |
|-----------|-----------|
| Arm title | treatment |
|-----------|-----------|

Arm description:

all subjects received treatment: Patients with relapse-relapsing multiple sclerosis (RRMS) were treated with TMP001 600mg twice daily over a treatment period of 24 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | TMP001 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

gelatin capsules, each containing 200 mg of the active drug substance, for oral administration at daily doses of up to 1200 mg in two divided doses over a period of 24 weeks

| Number of subjects in period 1 | treatment |
|--------------------------------|-----------|
| Started | 4 |
| Completed | 2 |
| Not completed | 2 |
| Consent withdrawn by subject | 1 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | treatment period |
|-----------------------|------------------|

Reporting group description:

patient included after screening

| Reporting group values | treatment period | Total | |
|--|------------------|-------|--|
| Number of subjects | 4 | 4 | |
| 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) | 4 | 4 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 2 | |
| Male | 2 | 2 | |
| height | | | |
| Units: meter | | | |
| arithmetic mean | 1.755 | | |
| standard deviation | ± 0.095 | - | |
| Body mass index | | | |
| Units: kilogram(s)/cubic metre | | | |
| arithmetic mean | 22.26 | | |
| standard deviation | ± 1.84 | - | |

End points

End points reporting groups

| | |
|--|-----------|
| Reporting group title | treatment |
| Reporting group description: all subjects received treatment: Patients with relapse-remitting multiple sclerosis (RRMS) were treated with TMP001 600mg twice daily over a treatment period of 24 weeks. | |

Primary: number of CEL lesions at weeks 12, 16, 20 and 24

| | |
|--|---|
| End point title | number of CEL lesions at weeks 12, 16, 20 and 24 ^[1] |
| End point description: Average total number of contrast enhancing lesions (CELs) on brain MRI scans at weeks 12, 16, 20, and 24 as compared to the average total number of CELs on brain MRI scans at week -4 and baseline (BL) | |
| End point type | Primary |
| End point timeframe: Baseline to week 12, 16, 20 and 24 | |

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: Since only a small number of patients could be enrolled statistical analysis was not feasible and was not done

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | treatment | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: number | | | | |
| number (not applicable) | | | | |

Notes:

[2] - not enough patients were included no summary could have been or has been done

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

run-in phase until end of treatment in week 24

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | treatment |
|-----------------------|-----------|

Reporting group description:

all patients that received a minimum of one dose of treatment

| Serious adverse events | treatment | | |
|---|---------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (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 | treatment | | |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|--|--|--|--|
| abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Musculoskeletal and connective tissue disorders Bursitis subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 1 / 4 (25.00%) 2 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 14 July 2015 | Protocol version 1.9 of 15.06.2015 Patient Information and Consent Form version 1.3 of 15.06.2015 Reasons: Additional information about an increased risk of cardiovascular side effects for NSAID Expanded inclusion and exclusion criteria Collection of coagulation status in the Safety Labor Change of a subinvestigator at an existing site |
| 17 September 2015 | Addition of new site |
| 19 January 2016 | Protocol version 2.0 of 14.01.2016 Protocol version 2.1 of 05.02.2016 Patient Information and Consent Form version 1.4 of 14.01.2016 Investigator's Brochure (IB) version 05 of 08.12.2015 IMPD version 2.0 of 19.01.2016 Reasons: Specification of the used MRI protocol Sensitivity of MRI was increased to detect lesions with feeble contrast agent enhancing abilities Investigator's Brochure (IB): Data from the phase I study with healthy volunteers were entered |
| 21 March 2016 | Addition of a new site |
| 07 September 2016 | Protocol version 3.0 of 03.08.2016 Patient Information and Consent Form version 2.0 of 03.08.2016 Patients Flyer version 1.1 of 18.08.2016 Reasons: Removal of brain MRIs on week 4 and week 8 New contact details |
| 07 March 2017 | Protocol version 4.0 of 02.03.2017 Investigator's brochure (IB) version 5.0 of 22.02.2017 Reasons: Extension of study duration until Q4/2017 Changes in the executive management of Fraunhofer IME Update Investigator's brochure (IB) |

Notes:

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.

only a small number of patients were enrolled in the study therefor no statistical analysis could be made.
Since all efforts for enable and facilitate recruitment failed study was closed.

Notes:

