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-remitting 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: