



Clinical trial results:

A multi-centre, open-label, phase 1 study, Part A single ascending dose and Part B multiple dose, to evaluate the safety, tolerability and pharmacokinetics, and to explore early signs of effectiveness of induction of antigen-specific immune tolerance with TPM203 in pemphigus vulgaris patients

Summary

EudraCT number	2019-001727-12
Trial protocol	DE
Global end of trial date	25 July 2023

Results information

Result version number	v1 (current)
This version publication date	26 March 2024
First version publication date	26 March 2024
Summary attachment (see zip file)	Synopsis (TPV11_CSR_v 1.0 _Synopsis_2023_12_04.pdf)

Trial information

Trial identification

Sponsor protocol code	TPV11
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Topas Therapeutics GmbH
Sponsor organisation address	Falkenried 88, Hamburg, Germany, 20251
Public contact	Cristina de Min, Topas Therapeutics GmbH, +49 40302089044, demin@topas-therapeutics.com
Scientific contact	Cristina de Min, Topas Therapeutics GmbH, +49 40302089044, demin@topas-therapeutics.com

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	04 December 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of the intravenous infusion of TPM203 in pemphigus vulgaris (PV) patients.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) for review and approval before study initiation. All revisions to the consent/assent forms after initial IEC approval were submitted by the investigator to the IEC for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	17
EEA total number of subjects	15

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)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 patients were included in the study: 13 patients were recruited in Germany, 2 patients were recruited in Italy and 2 patients in the United Kingdom.

Pre-assignment

Screening details:

Patients were included in cohorts, screening was done prior to each cohort

Period 1

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

Blinding implementation details:

Not applicable, open study

Arms

Are arms mutually exclusive?	Yes
Arm title	Single dose, dose level 1

Arm description:

Administration of TPM203 at a total dose of 0.12 umol

Arm type	Experimental
Investigational medicinal product name	TPM203
Investigational medicinal product code	TPM203
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile aqueous nanodispersion in glass vials, equimolar (based on peptide content) mixture of 4 TPCs (TPC0002, TPC0003, TPC0005, TPC0012) TPC. Dose level 1: 0.03 µmol peptide for each TPC (0.12 µmol total peptide). At each dose level, the TPCs were administered as a mixture of all four TPCs in a total volume of 20–28 ml nanodispersion (based on peptide content)

Arm title	Single dose, dose level 2
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Arm description:

Administration of TPM203 at a total dose of 0.36 umol

Arm type	Experimental
Investigational medicinal product name	TPM203
Investigational medicinal product code	TPM203
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile aqueous nanodispersion in glass vials, equimolar (based on peptide content) mixture of 4 TPCs (TPC0002, TPC0003, TPC0005, TPC0012). Dose level 2: 0.09 µmol peptide for each of the four TPCs (0.36 µmol total peptide). At each dose level, the TPCs were administered as a mixture of all four TPCs in a total volume of 20–28 ml nanodispersion (based on peptide content)

Arm title	Single dose, dose level 3
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Arm description:

Administration of TPM203 at a total dose of 1.2 umol

Arm type	Experimental
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Investigational medicinal product name	TPM203
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Sterile aqueous nanodispersion in glass vials, equimolar (based on peptide content) mixture of 4 TPCs (TPC0002, TPC0003, TPC0005, TPC0012). Dose level 3: 0.3 µmol peptide for each of the four TPCs (1.2 µmol total peptide). At each dose level, the TPCs were administered as a mixture of all four TPCs in a total volume of 20–28 ml nanodispersion (based on peptide content)

Arm title	Single dose, dose level 4
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Arm description:

Administration of TPM203 at a total dose of 3.6 umol

Arm type	Experimental
Investigational medicinal product name	TPM203
Investigational medicinal product code	TPM203
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile aqueous nanodispersion in glass vials, equimolar (based on peptide content) mixture of 4 TPCs (TPC0002, TPC0003, TPC0005, TPC0012). Dose level 4: 0.9 µmol peptide for each of the four TPCs (3.6 µmol total peptide). At each dose level, the TPCs were administered as a mixture of all four TPCs in a total volume of 20–28 ml nanodispersion (based on peptide content)

Arm title	Multiple Doses (Three doses)
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Arm description:

Administration of three doses of TPM203 at a dose of 3.6 umol per dose

Arm type	Experimental
Investigational medicinal product name	TPM203
Investigational medicinal product code	TPM203
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile aqueous nanodispersion in glass vials, equimolar (based on peptide content) mixture of 4 TPCs (TPC0002, TPC0003, TPC0005, TPC0012). Multiple does, total peptide 3.6 mmol. At each dose level, the TPCs were administered as a mixture of all four TPCs in a total volume of 20–28 ml nanodispersion (based on peptide content)

Number of subjects in period 1	Single dose, dose level 1	Single dose, dose level 2	Single dose, dose level 3
Started	3	3	3
Completed	3	3	3

Number of subjects in period 1	Single dose, dose level 4	Multiple Doses (Three doses)
Started	3	5
Completed	3	5

Baseline characteristics

Reporting groups	
Reporting group title	Single dose, dose level 1
Reporting group description: Administration of TPM203 at a total dose of 0.12 umol	
Reporting group title	Single dose, dose level 2
Reporting group description: Administration of TPM203 at a total dose of 0.36 umol	
Reporting group title	Single dose, dose level 3
Reporting group description: Administration of TPM203 at a total dose of 1.2 umol	
Reporting group title	Single dose, dose level 4
Reporting group description: Administration of TPM203 at a total dose of 3.6 umol	
Reporting group title	Multiple Doses (Three doses)
Reporting group description: Administration of three doses of TPM203 at a dose of 3.6 umol per dose	

Reporting group values	Single dose, dose level 1	Single dose, dose level 2	Single dose, dose level 3
Number of subjects	3	3	3
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean standard deviation	47.0 ± 18.08	50.3 ± 12.22	57.0 ± 5.00
Gender categorical Units: Subjects			
Female	1	3	2
Male	2	0	1

Reporting group values	Single dose, dose level 4	Multiple Doses (Three doses)	Total
Number of subjects	3	5	17
Age categorical 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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	58.7	52.4	
standard deviation	± 8.74	± 7.23	-
Gender categorical			
Units: Subjects			
Female	1	2	9
Male	2	3	8

End points

End points reporting groups

Reporting group title	Single dose, dose level 1
Reporting group description: Administration of TPM203 at a total dose of 0.12 umol	
Reporting group title	Single dose, dose level 2
Reporting group description: Administration of TPM203 at a total dose of 0.36 umol	
Reporting group title	Single dose, dose level 3
Reporting group description: Administration of TPM203 at a total dose of 1.2 umol	
Reporting group title	Single dose, dose level 4
Reporting group description: Administration of TPM203 at a total dose of 3.6 umol	
Reporting group title	Multiple Doses (Three doses)
Reporting group description: Administration of three doses of TPM203 at a dose of 3.6 umol per dose	

Primary: Safety and tolerability

End point title	Safety and tolerability ^[1]
End point description: No serious adverse event, no IMP-related discontinuation and no adverse event of special interest has been reported in the trial. No safety signal has been identified, specifically not related to any of the anticipated potential risks	
End point type	Primary
End point timeframe: Safety and tolerability data were collected from signature of informed consent until last visit.	

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: Safety and tolerability are primary endpoints. Descriptive statistics only.

End point values	Single dose, dose level 1	Single dose, dose level 2	Single dose, dose level 3	Single dose, dose level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Not applicable				
Safety and tolerability	0	0	0	0

End point values	Multiple Doses (Three doses)			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Not applicable				
Safety and tolerability	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from informed consent until the patient's last visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	Intention to treat
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Reporting group description: -

Serious adverse events	Intention to treat		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (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	Intention to treat		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Condition aggravated			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	7		
Fatigue			

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2		
Feeling cold subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2		
Infusion site pain subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 4		
Unevaluable event subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 10		
Immune system disorders Lower respiratory tract infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Investigations Blood pressure increased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Injury, poisoning and procedural complications			

Fall subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Immunisation reaction subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Cardiac disorders Sinus arrhythmia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	7 / 17 (41.18%) 8		
Paraesthesia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hypochromic anaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Lymphopenia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Flatulence subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		

Lip erosion subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Lip swelling subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Nausea subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Oral blood blister subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Oral dysaesthesia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Oral mucosa erosion subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Tongue coated subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Back pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		

Influenza			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Laryngitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2019	Amendment 1 incorporated the changes requested by the German Health Authorities and the Leading EC in Marburg, respectively, and were implemented before screening of any patient was initiated.
29 October 2019	Amendment 2 incorporated the changes requested by the German Health Authorities and the Leading EC in Marburg, respectively, and were implemented before screening of any patient was initiated.
28 February 2020	Amendment 3 incorporated corrections and clarifications based on the experience gathered screening and treating the first patient, including the following: <ul style="list-style-type: none">- the interval mandating a Screening Confirmation Visit was prolonged from 8 to 12 weeks,- the upper limit of the body mass index was set to ≤ 32, instead of ≤ 30- the usage of steroids other than prednisolone was clarified.
16 June 2020	Amendment 4 incorporated a SARS-CoV-2 infection / COVID-19 risk assessment, the implementation of adequate measures to minimize the SARS-CoV-2 infection risk and rules to prevent an IMP administration to a SARS-CoV-2 infected patient.
11 October 2020	Because of recruitment difficulties, the study was extended to include additional German sites as well as additional international clinical sites with Amendment 5
02 November 2021	Amendment 6 incorporated the use of additional methods for detection of anti-Dsg3 serum IgG and the inclusion of patients carrying HLA-DRB1*04:02 and/or HLA-DQB1*05:03. The permitted use of systemic corticosteroids was adjusted to body weight. The collection of patients' sera for analysis of anti-Dsg3 IgG antibodies was extended for 3 month and SARS-CoV-2 specific rules were adjusted to current pandemic status.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported