Clinical trial results:
A Phase III Open-label Extension Study to Evaluate Long-term Safety and Efficacy of PRM-151 in Patients with Idiopathic Pulmonary Fibrosis (IPF)

Summary

EudraCT number	2020-001429-30
Trial protocol	FR CZ DE SE GR HU PT AT FI NO DK PL NL BE IT
Global end of trial date	10 February 2023

Results information

Result version number	v2
This version publication date	06 April 2024
First version publication date	18 February 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	WA42294

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04594707
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	10 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was evaulating the long-term safety, efficacy and pharmacokinetics (PK) of recombinant human pentraxin-2 (rhPTX-2; PRM-151) zinpentraxin alfa, administered by intravenous (IV) infusion to participants with idiopathic pulmonary fibrosis (IPF).

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 2021
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	Australia: 10
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	117
EEA total number of subjects	52

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)	11
From 65 to 84 years	102
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled across 48 investigative sites in 16 countries.

Pre-assignment

Screening details:

This OLE study enrolled eligible participants with IPF who took part in the Phase II Study PRM-151-202/WA42404 or and Phase III Study WA42293.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Zinpentraxin Alfa

Arm description:

Participants entered this Cohort following participation in study PRM-151-202.

Arm type	Experimental
Investigational medicinal product name	Zinpentraxin Alfa
Investigational medicinal product code	
Other name	PRM-151
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants receiveD three loading doses of open-label PRM-151 on days 1, 3, and 5, then one infusion every 4 weeks (Q4W). 10 mg/kg of PRM 151 will be administered by intravenous (IV) infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks.

Arm title	Cohort B: Ex-Placebo

Arm description:

Participants entered, following participation in study WA42293.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo matching Zinpentraxin Alfa administered by IV infusion on Days 1, 3 and 5, followed by infusions Q4W until the end of the study.

Arm title	Cohort B: Zinpentraxin Alfa

Arm description:

Participants entered, following participation in study WA42293.

Arm type	Experimental

Investigational medicinal product name	Zinpentraxin Alfa
Investigational medicinal product code	
Other name	PRM-151
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants previously randomized to the placebo in WA42293 received study medication in the three loading doses on days 1, 3 and 5 in a blinded fashion. All three doses contained PRM-151. Participants previously randomized to the treatment arm in WA42293 received study medication in the three loading doses on days 1, 3 and 5 in a blinded fashion. One of the three doses contained PRM-151, whereas two doses contained placebo.

Number of subjects in period 1	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa
Started	21	49	47
Completed	0	0	0
Not completed	21	49	47
Consent withdrawn by subject	1	-	2
Lung Transplant	-	-	1
Grade 4 infusion related reaction (IRR)	1	-	-
Adverse Event	-	-	1
Study Terminated By Sponsor	19	47	41
Death	-	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: Zinpentraxin Alfa
Reporting group description:	
Participants entered this Cohort following participation in study PRM-151-202.	
Reporting group title	Cohort B: Ex-Placebo
Reporting group description:	
Participants entered, following participation in study WA42293.	
Reporting group title	Cohort B: Zinpentraxin Alfa
Reporting group description:	
Participants entered, following participation in study WA42293.	

Reporting group values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa
Number of subjects	21	49	47
Age Categorical 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)	1	4	6
From 65-84 years	20	42	40
85 years and over	0	3	1
Age Continuous Units: years			
arithmetic mean	74.5	74.6	73.2
standard deviation	± 5.5	± 7.6	± 6.8
Gender Categorical Units: Subjects			
Female	5	10	10
Male	16	39	37
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	2	2
Not Hispanic or Latino	18	47	45
Race (NIH/OMB) Units: Subjects			
Asian	0	0	1
Black or African American	1	1	0
White	19	47	43
Multiple	0	0	1
Unknown	1	1	2

Reporting group values	Total		

Number of subjects	117		
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)	11		
From 65-84 years	102		
85 years and over	4		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	25		
Male	92		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7		
Not Hispanic or Latino	110		
Race (NIH/OMB) Units: Subjects			
Asian	1		
Black or African American	2		
White	109		
Multiple	1		
Unknown	4		

End points

End points reporting groups

Reporting group title	Cohort A: Zinpentraxin Alfa
Reporting group description:	
Participants entered this Cohort following participation in study PRM-151-202.	
Reporting group title	Cohort B: Ex-Placebo
Reporting group description:	
Participants entered, following participation in study WA42293.	
Reporting group title	Cohort B: Zinpentraxin Alfa
Reporting group description:	
Participants entered, following participation in study WA42293.	

Primary: Percentage of Participants with Adverse Events (AE)

End point title	Percentage of Participants with Adverse Events (AE)[1]
End point description:	
An AE was defined as any untoward medical occurrence in a clinical investigation participant who was administered a pharmaceutical product, regardless of causal attribution. Grading was completed according to the CTCAE, version 5.0. The safety-evaluable population included all enrolled participants who received at least one administration (full or partial dose) of study drug.	
End point type	Primary
End point timeframe:	
From baseline until 8 weeks after the final dose, an average of 6 months	

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: The analysis of this safety endpoint would just be "descriptive summary of incidence of AEs"

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Percentage of participants				
number (not applicable)	85.7	51.0	55.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Infusion Related Reactions (IRRs) and other AEs of Special Interest

End point title	Percentage of Participants with Infusion Related Reactions (IRRs) and other AEs of Special Interest

End point description:

IRRs were defined as AEs that occurred during or within 24 hours after study drug administration and were judged to be related to study drug infusion.
The safety-evaluable population included all enrolled participants who received at least one

administration (full or partial dose) of study drug.

End point type	Secondary

End point timeframe:

From baseline until 8 weeks after the final dose, an average of 6 months

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Percentage of participants				
number (not applicable)	9.5	4.1	8.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Rate of Change in Forced Vital Capacity (FVC) (mL)

End point title	Annual Rate of Change in Forced Vital Capacity (FVC) (mL)

End point description:

The full analysis set included all enrolled participants who received at least one administration (full or partial dose) of study drug.

End point type	Secondary

End point timeframe:

From baseline until study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Milliliter (mL)				
arithmetic mean (confidence interval 95%)	-229.12 (-317.39 to 140.9)	-272.96 (-698.97 to 153.06)	-120.77 (-546.26 to 294.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of of Participants Permanently Discontinuing Study Treatment due to AEs

End point title	Percentage of of Participants Permanently Discontinuing Study

	Treatment due to AEs

End point description:

The safety-evaluable population included all enrolled participants who received at least one administration (full or partial dose) of study drug.

End point type	Secondary

End point timeframe:

From baseline until 8 weeks after the final dose, an average of 6 months

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Percentage of of participants				
number (not applicable)	9.5	4.1	2.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Carbon Monoxide Diffusing Capacity (DLCO)

End point title	Change in Carbon Monoxide Diffusing Capacity (DLCO)

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization. In the Ex-placebo arm, no participant was assessed for DLCO after baseline. 9999999 = Due to short length of follow-up, no DLCO assessment was collected at Week 48. At week 24, the standard deviation for Cohort B: Zinpentraxin Alfa could not be calculated from the data of 1 participant.

End point type	Secondary

End point timeframe:

At Baseline, Week 24 and Week 48

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	36	28	
Units: DLCO% Predicted				
arithmetic mean (standard deviation)				
Baseline (n=11,36,28)	40.20 (± 16.29)	44.91 (± 10.94)	42.27 (± 11.14)	
Week 24 (n=5,0,1)	1.08 (± 4.05)	9999999 (± 9999999)	-1.55 (± 9999999)	
Week 48 (n=5,0,0)	-2.80 (± 3.76)	9999999 (± 9999999)	9999999 (± 9999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Rate of Change in 6-Minute Walk Distance (6MWD)

End point title	Annual Rate of Change in 6-Minute Walk Distance (6MWD)

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization.

End point type	Secondary

End point timeframe:

From baseline until study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Meters (m)				
arithmetic mean (confidence interval 95%)	-86.95 (-170.80 to -3.10)	64.64 (-98.62 to 227.90)	-163.66 (-324.02 to -3.30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Rate of Change in FVC% Predicted

End point title	Annual Rate of Change in FVC% Predicted

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization.

End point type	Secondary

End point timeframe:

From baseline until study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Percent predicted				
arithmetic mean (confidence interval 95%)	-6.96 (-9.70 to -4.22)	-6.91 (-14.77 to 0.96)	-3.37 (-11.18 to 4.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression

End point title	Time to Disease Progression

End point description:

Time to first occurrence of >=10% absolute decline in % predicted FVC, >=15% relative decline in 6MWD, or death. The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization. 9999999 = Due to the low number of events and early termination of the study, the median and 95% CI weren't estimable.

End point type	Secondary

End point timeframe:

From baseline until study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Months				
number (confidence interval 95%)	5.6 (2.9 to 8.3)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Survival

End point title	Survival

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization. 9999999 = Due to the low number of events, the median and 95% CI was not estimable.

End point type	Secondary

End point timeframe:

Every 6 Months and at study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Months				
number (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: IPF-related Mortality

End point title	IPF-related Mortality

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization. 9999999 = Due to the low number of events, the median and 95% CI was not estimable.

End point type	Secondary

End point timeframe:

Every 6 Months and at study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Months				
median (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Respiratory-related Mortality

End point title	Respiratory-related Mortality

End point description:

The full analysis set included all randomized participants who received at least one administration (full or partial dose) of study drug and used the grouping according to the treatment assignment at randomization. 9999999 = Due to the low number of events, the median and 95% CI was not estimable.

End point type	Secondary

End point timeframe:

Every 6 Months and at study completion (up to approximately 1.5 years)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	49	47	
Units: Months				
median (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of PRM-151 at Specified Timepoints

End point title	Plasma Concentrations of PRM-151 at Specified Timepoints[2]

End point description:

The pharmacokinetic population included all randomized participants who received at least one administration (full or partial dose) of zinpentraxin alfa and at least one evaluable postdose PK sample that was above the lower limit of quantification (LLOQ). 9999999 =At Baseline, no drug had been administered. Thus, there is no data to record for the plasma concentration of zinpentraxin alfa.

End point type	Secondary

End point timeframe:

Days 1 and 5, Weeks 4, and 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Due to early termination of the study, only participants enrolled in Cohort A receiving at least one IV dose of zinpentraxin alfa had their plasma concentrations analyzed.

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Zinpentraxin Alfa		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	0[3]		
Units: micrograms per millilitre (ug/mL)				
arithmetic mean (standard deviation)				
Day 1 -pre infusion (n=0)	9999999 (± 9999999)	()		
Day 1 - 2h Post Infusion (n=210)	203.85 (± 55.72)	()		

Day 5 - Pre Infusion (n=21)	42.83 (± 18.89)	()		
Day 5 - 2h Post Infusion (n=20)	252.90 (± 53.42)	()		
Week 4 - Pre Infusion (n=18)	2.50 (± 0)	()		
Week 4 - 2h Post Infusion (n=18)	209.00 (± 42.93)	()		
Week 12 - Pre Infusion (n=17)	2.50 (± 0)	()		
Week 12 - 2h Post Infusion (n=17)	215.65 (± 50.47)	()		

Notes:

[3] - Only participants in Cohort A who received at least one IV dose of zinpentraxin alfa were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Prevalence of Anti-drug Antibodies (ADAs) to PRM-151 at Baseline

End point title	Prevalence of Anti-drug Antibodies (ADAs) to PRM-151 at Baseline

End point description:

Due to early termination of the study, only ADA samples from participants in Cohort A were analyzed. The immunogenicity population included all randomized participants with at least one post-dose ADA assessment and were grouped according to treatment received or, if no treatment is received prior to study discontinuation, according to treatment assigned.

End point type	Secondary

End point timeframe:

Baseline (Day 1)

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	0[4]	0[5]	
Units: Participants				
number (not applicable)	0			

Notes:

[4] - Due to early termination of the study, only ADA samples from participants in Cohort A were analyzed.

[5] - Due to early termination of the study, only ADA samples from participants in Cohort A were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ADAs During the Study

End point title	Percentage of Participants with ADAs During the Study

End point description:

The immunogenicity population included all randomized participants with at least one postdose ADA assessment and were grouped according to treatment received or, if no treatment is received prior to study discontinuation, according to treatment assigned.

End point type	Secondary

End point timeframe:
Weeks 4, 12 and 24

End point values	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	0[6]	0[7]	
Units: Percentage of participants				
number (not applicable)	0			

Notes:

[6] - Due to early termination of the study, only ADA samples from participants in Cohort A were analyzed.
[7] - Due to early termination of the study, only ADA samples from participants in Cohort A were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline until 8 weeks after the final dose, an average of 6 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Cohort A: Zinpentraxin Alfa
Reporting group description:	
Participants entered this Cohort following participation in study PRM-151-202.	
Reporting group title	Cohort B: Ex-Placebo
Reporting group description:	
Participants entered, following participation in study WA42293.	
Reporting group title	Cohort B: Zinpentraxin Alfa
Reporting group description:	
Participants entered, following participation in study WA42293.	

Serious adverse events	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 21 (23.81%)	8 / 49 (16.33%)	6 / 47 (12.77%)
number of deaths (all causes)	0	2	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon neoplasm			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Microscopic polyangiitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 21 (0.00%)	2 / 49 (4.08%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Vascular stent thrombosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 21 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 21 (4.76%)	2 / 49 (4.08%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 49 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 49 (2.04%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 49 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort A: Zinpentraxin Alfa	Cohort B: Ex-Placebo	Cohort B: Zinpentraxin Alfa
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 21 (66.67%)	16 / 49 (32.65%)	14 / 47 (29.79%)
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	2 / 21 (9.52%)	2 / 49 (4.08%)	4 / 47 (8.51%)
occurrences (all)	3	4	4
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 21 (9.52%)	3 / 49 (6.12%)	0 / 47 (0.00%)
occurrences (all)	3	3	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	3 / 49 (6.12%)	3 / 47 (6.38%)
occurrences (all)	1	3	4
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	5 / 21 (23.81%)	0 / 49 (0.00%)	2 / 47 (4.26%)
occurrences (all)	5	0	2
Sinus congestion			
subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Cough			
subjects affected / exposed	0 / 21 (0.00%)	1 / 49 (2.04%)	3 / 47 (6.38%)
occurrences (all)	0	1	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 21 (19.05%)	6 / 49 (12.24%)	4 / 47 (8.51%)
occurrences (all)	4	6	4
Acute sinusitis			

subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
subjects affected / exposed	2 / 21 (9.52%)	3 / 49 (6.12%)	2 / 47 (4.26%)
occurrences (all)	2	3	2
Lower respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	4 / 49 (8.16%)	1 / 47 (2.13%)
occurrences (all)	1	4	1
Metabolism and nutrition disorders			
Vitamin B12 deficiency			
subjects affected / exposed	2 / 21 (9.52%)	0 / 49 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2020	This protocol was amended for the following reasons: 1) PK samples were to be collected as plasma instead of serum; 2) Participants in Cohort had all 3 initial loading doses blinded; 3) Clarification of the formulation of PRM-151; 4) Clarification that for loading or reloading doses, scheduled efficacy assessments would only be performed on the first of the three loading dose days; 5) Information regarding acute or suspected acute IPF exacerbation did not need to be recorded on the eCRF, instead be reported as an AE or SAE; 6) Serious hypersensitivity reactions and Grade 4 infusion-related reaction (IRR) or two Grade 3 IRRs were added as reasons for permanent study treatment discontinuation; 7) Sections on exploratory biomarker research and blood sample collection for genome or exome sequencing were removed; 8) Clarification that in order to consider treatment discontinuation after two Grade 3IRRs, the first occurrence of the Grade 3 IRR can be either in the Phase II Study PRM-151-202, Phase III Study WA42293 or in this study; 9) Acute or suspected exacerbation of idiopathic pulmonary fibrosis (IPF) has been added as an AESI; 10) Clarification that the safety evaluable population include all randomized participants who received at least one administration (full or partial dose) of study drug; 11) An iDMC was employed to review safety data from this study only up until the time the database for primary analysis for Study WA42293 was locked, and Study WA42293 was unblinded to the Sponsor; 12) Appendices were updated with the latest versions of the documents.
01 February 2022	Additional text was added to the protocol.
28 April 2022	Additional text was added to the protocol in this amendment to describe the following: the galectin-1 and galectin-3 host cell protein identified within first generation PRM-151 drug product, the sugar galactose- -1,3-galactose identified in first and second generation PRM-151 drug product and on the increased risk, and the potential risk of post-implantation fetal loss associated with PRM-151.

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.

This study was terminated early due to the Sponsor's decision to terminate the parent study early.

Notes: