Clinical trial results:
A Phase III Randomized, Double-blind, Placebo Controlled Trial to Evaluate the Efficacy and Safety of PRM-151 in Patients with Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2020-000791-38
Trial protocol	SE CZ DE HU GR FI PT NO DK PL NL BE IT
Global end of trial date	10 February 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	WA42293

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04552899
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 phase III study was to evaluate the efficacy, safety and pharmacokinetics (PK) of recombinant human pentraxin-2 (rhPTX-2; PRM-151) zinpentraxin alfa, compared with placebo in 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	17 March 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 13
Country: Number of subjects enrolled	Australia: 44
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	China: 27
Country: Number of subjects enrolled	Czechia: 10
Country: Number of subjects enrolled	Germany: 30
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	France: 50
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Greece: 18
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Israel: 35
Country: Number of subjects enrolled	Italy: 57
Country: Number of subjects enrolled	Japan: 41
Country: Number of subjects enrolled	Korea, Republic of: 24
Country: Number of subjects enrolled	Netherlands: 13

Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 156
Country: Number of subjects enrolled	South Africa: 4
Worldwide total number of subjects	664
EEA total number of subjects	276

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)	128
From 65 to 84 years	531
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

A total of 665 participants were enrolled across 275 investigative sites in 29 countries.

Pre-assignment

Screening details:

One participant who failed screening was enrolled in error and did not subsequently enter the study. Four participants who were randomized did not receive any treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Zinpentraxin Alfa

Arm description:

Participants received intravenous (IV) infusions of Zinpentraxin Alfa over 50-70 minutes on Days 1, 3 and 5, then followed by infusions every 4 weeks (Q4W) to Week 48.

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 a 10 mg/kg intravenous (IV) infusions of Zinpentraxin Alfa based on the participants weight. It was administered on Days 1, 3 and 5 followed by infusions Q4W to Week 48.

Arm title	Placebo

Arm description:

Participants received IV infusions of placebo over 50-70 minutes on Days 1, 3 and 5, followed by infusions Q4W to Week 48.

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 to Week 48.

Number of subjects in period 1	Zinpentraxin Alfa	Placebo
Started	331	333
No Treatment	1 [1]	3 [2]
Completed	56	49
Not completed	275	284
Lung Transplant	4	3
Physician decision	3	4
Consent withdrawn by subject	15	17
Adverse Event	4	3
Study Terminated By Sponsor	237	239
Death	4	4
Participant and physician wanted to withdraw	-	1
Lost to follow-up	8	13

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These participants were randomized but didn't receive any study treatment.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: These participants were randomized but didn't receive any study treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Zinpentraxin Alfa
Reporting group description:	
Participants received intravenous (IV) infusions of Zinpentraxin Alfa over 50-70 minutes on Days 1, 3 and 5, then followed by infusions every 4 weeks (Q4W) to Week 48.	
Reporting group title	Placebo
Reporting group description:	
Participants received IV infusions of placebo over 50-70 minutes on Days 1, 3 and 5, followed by infusions Q4W to Week 48.	

Reporting group values	Zinpentraxin Alfa	Placebo	Total
Number of subjects	331	333	664
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)	64	64	128
From 65-84 years	266	265	531
85 years and over	1	4	5
Age Continuous Units: years			
arithmetic mean	70.8	70.6	
standard deviation	± 7.3	± 7.6	-
Gender Categorical Units: Subjects			
Female	61	70	131
Male	270	263	533
Race (NIH/OMB) Units: Subjects			
Asian	52	56	108
Black or African American	1	4	5
White	274	270	544
Multiple	1	0	1
Unknown	3	3	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	20	27	47
Not Hispanic or Latino	302	299	601
Not Stated	6	6	12
Unknown	3	1	4

End points

End points reporting groups

Reporting group title	Zinpentraxin Alfa
Reporting group description:	
Participants received intravenous (IV) infusions of Zinpentraxin Alfa over 50-70 minutes on Days 1, 3 and 5, then followed by infusions every 4 weeks (Q4W) to Week 48.	
Reporting group title	Placebo
Reporting group description:	
Participants received IV infusions of placebo over 50-70 minutes on Days 1, 3 and 5, followed by infusions Q4W to Week 48.	

Primary: Absolute Change in Forced Vital Capacity (FVC [mL])

End point title	Absolute Change in Forced Vital Capacity (FVC [mL])
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	Primary
End point timeframe:	
From Baseline up to Week 52	

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Milliliters (mL)				
arithmetic mean (confidence interval 95%)	-235.72 (-283.07 to -188.4)	-214.89 (-262.44 to -167.3)		

Statistical analyses

Statistical analysis title	Difference in Change from Baseline at Week 52
Comparison groups	Zinpentraxin Alfa v Placebo
Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.54
Method	Random Coefficient Regression Model
Parameter estimate	Difference in Change from Baseline
Point estimate	-20.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	-87.94
upper limit	46.29
Variability estimate	Standard error of the mean
Dispersion value	34.11

Secondary: Time to First Respiratory-related Hospitalizations

End point title	Time to First Respiratory-related Hospitalizations

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 = Not enough events available for estimation.

End point type	Secondary

End point timeframe:

From Baseline up to 1 year

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Months				
median (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	Zinpentraxin Alfa
Comparison groups	Zinpentraxin Alfa v Placebo
Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9833
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.97

Secondary: Time to Disease Progression

End point title	Time to Disease Progression

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 up to 1 year

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Months				
median (confidence interval 95%)	6.6 (5.6 to 9.1)	8.2 (6.5 to 10.9)		

Statistical analyses

Statistical analysis title	Zinpentraxin Alfa
Comparison groups	Zinpentraxin Alfa v Placebo
Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2512
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.47

Secondary: Absolute Change in FVC% Predicted

End point title	Absolute 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 up to Week 52

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Percent predicted				
arithmetic mean (confidence interval 95%)	-6.22 (-7.46 to -4.98)	-5.72 (-6.96 to -4.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change in 6-minute Walk Distance (6MWD)

End point title	Absolute 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 up to Week 52

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Meters (m)				
arithmetic mean (confidence interval 95%)	-33.64 (-48.71 to -18.57)	-24.19 (-39.29 to -9.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in St. George Respiratory Questionnaire (SGRQ) Total Score

End point title	Change in St. George Respiratory Questionnaire (SGRQ) Total Score

End point description:

The SGRQ is a 50-item respiratory-specific quality-of-life questionnaire. The questions assess the impact of disease on activity, functionality and symptoms. Each scale is scored from 0-100. A total score represents the weighted average of these three subscores. A lower score indicates best health while a

higher score indicates worst health.

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:

At Baseline, Week 12, Week 24, Week 36 and Week 52

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	299		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=229, 299)	36.73 (± 18.63)	37.66 (± 18.45)		
Week 12 (n=172, 179)	1.03 (± 9.98)	0.81 (± 10.55)		
Week 24 (n=121, 122)	3.50 (± 11.05)	1.39 (± 13.94)		
Week 36 (n=110, 110)	3.21 (± 11.38)	2.15 (± 13.42)		
Week 52 (n=46, 43)	6.15 (± 13.87)	3.09 (± 11.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in University of California, San Diego-Shortness of Breath Questionnaire (UCSD-SOBQ)

End point title	Change in University of California, San Diego-Shortness of Breath Questionnaire (UCSD-SOBQ)

End point description:

The UCSD-SOBQ is a 24-item questionnaire used to assess dyspnea severity during specific activities (21 items) and limitations caused by dyspnea in daily life (4 items). Items are assessed using a 6-point scale. Total scores, once summed, can range from 0-120 with a higher score reflecting greater dyspnea severity. 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:

At Baseline, Week 12, Week 24, Week 36 and Week 52

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	271		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=276, 271)	28.9 (± 22.2)	29.9 (± 22.6)		
Week 12 (n=147, 151)	0.8 (± 13.0)	4.0 (± 17.4)		
Week 24 (n=106, 110)	3.2 (± 16.0)	4.7 (± 16.8)		
Week 36 (n=97, 96)	5.4 (± 17.5)	6.9 (± 17.7)		
Week 52 (n=37, 35)	11.1 (± 21.2)	4.8 (± 14.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Acute Exacerbation of Idiopathic Pulmonary Fibrosis (IPF)

End point title	Time to First Acute Exacerbation of Idiopathic Pulmonary Fibrosis (IPF)

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 = Not enough events available for estimation.

End point type	Secondary

End point timeframe:

From Baseline up to 1 year

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Months				
median (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	Zinpentraxin Alfa
Comparison groups	Zinpentraxin Alfa v Placebo

Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7005
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.86

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.

End point type	Secondary

End point timeframe:

At Baseline, Week 12, Week 24, Week 36 and Week 52

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	313		
Units: DLCO% Predicted				
arithmetic mean (standard deviation)				
Baseline (n=318, 313)	51.73 (± 17.73)	51.66 (± 14.78)		
Week 12 (n=153, 165)	-1.19 (± 11.89)	-2.78 (± 9.86)		
Week 24 (n=110, 108)	-4.68 (± 7.93)	-4.01 (± 9.75)		
Week 36 (n=95, 90)	-5.83 (± 8.49)	-4.66 (± 7.10)		
Week 52 (n=32, 36)	-6.30 (± 9.56)	-6.68 (± 9.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Infusion-related Reactions (IRRs) and Other Adverse Events of Special Interest

End point title	Percentage of Participants with Infusion-related Reactions (IRRs) and Other Adverse Events of Special Interest

End point description:

The safety population included all randomized participants who received at least one administration (full or partial dose) of study drug and were grouped according to the actual treatment received.

End point type	Secondary

End point timeframe:

From Baseline up to 8 weeks after the last dose of study drug (up to an average of 1 year)

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	329		
Units: Percentage of participants				
number (not applicable)	3.6	1.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events (AEs)

End point title	Percentage of Participants with Adverse Events (AEs)

End point description:

The safety population included all randomized participants who received at least one administration (full or partial dose) of study drug and were grouped according to the actual treatment received.

End point type	Secondary

End point timeframe:

From Baseline up to 8 weeks after the last dose of study drug (up to an average of 1 year)

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	329		
Units: Percentage of participants				
number (not applicable)	74.6	72.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival

End point title	Survival

End point description:

Survival is measured by all-cause mortality. 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 = Not enough events available for estimation.

End point type	Secondary

End point timeframe:

From Baseline up to 1 year

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Months				
median (confidence interval 95%)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of PRM-151

End point title	Plasma Concentrations of PRM-151[1]

End point description:

The pharmacokinetic (PK) 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 = NA. At Baseline, no drug had been administered. Thus, there is no data to record for the plasma concentration of zinpentraxin alfa.
9999999 = NA at Weeks, 4, 12 and 24 pre infusion as the drug level was below the limit of quantification of the assay.

End point type	Secondary

End point timeframe:

Days 1, 5 and Weeks 4, 12, and 24

Notes:

[1] - 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: The placebo group didn't receive the study drug, thus was no eligible to be analyzed for this endpoint.

End point values	Zinpentraxin Alfa			
Subject group type	Reporting group			
Number of subjects analysed	310			
Units: micrograms per millilitre (ug/mL)				
arithmetic mean (standard deviation)				
Day 1 -pre infusion (n=0)	9999999 (± 9999999)			
Day 1 - 1h Post Infusion (n=33)	198 (± 56.8)			
Day 1 - 2h Post Infusion (n=310)	203 (± 68.4)			
Day 1 - 4h Post Infusion (n=33)	168 (± 48.0)			

Day 1 - 8h Post Infusion (n=15)	118 (± 37.8)			
Day 1 - 10h Post Infusion (n=18)	158 (± 35.8)			
Day 1 - 12h Post Infusion (n=15)	95.9 (± 31.5)			
Day 1 - 24h Post Infusion (n=33)	81.8 (± 26.2)			
Day 5 - Pre Infusion (n=303)	39.6 (± 21.5)			
Day 5 - 2h Post Infusion (n=301)	244 (± 75.6)			
Week 4 - Pre Infusion (n=276)	9999999 (± 9999999)			
Week 4 - 2h Post Infusion (n=280)	212 (± 105)			
Week 12 - Pre Infusion (n=180)	9999999 (± 9999999)			
Week 12 - 2h Post Infusion (n=180)	177 (± 72.7)			
Week 24 - Pre Infusion (n=133)	9999999 (± 9999999)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants Permanently Discontinuing Study Treatment due to AEs

End point description:

The safety population included all randomized participants who received at least one administration (full or partial dose) of study drug and were grouped according to the actual treatment received.

End point type	Secondary

End point timeframe:

From Baseline up to 8 weeks after the last dose of study drug (up to an average of 1 year)

End point values	Zinpentraxin Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	329		
Units: Percentage of participants				
number (not applicable)	2.7	1.8		

Statistical analyses

No statistical analyses for this end point

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

End point title	Prevalence of Anti-drug Antibodies (ADAs) at Baseline[2]

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. There is no data reported for the Placebo Arm as that group never received any study drug. As such, we cannot measure anti-drug antibodies for that group of participants.

End point type	Secondary

End point timeframe:

At Baseline

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: The placebo group didn't receive the study drug, thus was no eligible to be analyzed for this endpoint.

End point values	Zinpentraxin Alfa			
Subject group type	Reporting group			
Number of subjects analysed	255			
Units: Participants				
number (not applicable)	0			

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[3]

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. There is no data reported for the Placebo Arm as that group never received any study drug. As such, we cannot measure anti-drug antibodies for that group of participants.

End point type	Secondary

End point timeframe:

Days 1, 5 and Weeks 4, 12, 24, 36, 48, 52 and 56

Notes:

[3] - 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: The placebo group didn't receive the study drug, thus was no eligible to be analyzed for this endpoint.

End point values	Zinpentraxin Alfa			
Subject group type	Reporting group			
Number of subjects analysed	280			
Units: Percentage of participants				
number (not applicable)	1.1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 8 weeks after the last dose of study drug (up to an average of 1 year)

Adverse event reporting additional description:

Total # of deaths was reported based on randomized population =all randomized participants.

SAEs & other AEs reported based on safety-evaluable population which included all randomized participants who received at least one administration (full or partial dose) of study drug and were grouped according to the actual treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received IV infusions of placebo over 50-70 minutes on Days 1, 3 and 5, followed by infusions Q4W to Week 48.

Reporting group title	Zinpentraxin Alfa

Reporting group description:

Participants received intravenous (IV) infusions of Zinpentraxin Alfa over 50-70 minutes on Days 1, 3 and 5, then followed by infusions every 4 weeks (Q4W) to Week 48.

Serious adverse events	Placebo	Zinpentraxin Alfa	
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 329 (12.16%)	46 / 331 (13.90%)	
number of deaths (all causes)	4	5	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-small cell lung cancer			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microscopic polyangiitis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 329 (0.00%)	2 / 331 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 329 (0.30%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	3 / 329 (0.91%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute respiratory failure			
subjects affected / exposed	0 / 329 (0.00%)	2 / 331 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	8 / 329 (2.43%)	12 / 331 (3.63%)	
occurrences causally related to treatment / all	0 / 8	1 / 12	
deaths causally related to treatment / all	0 / 3	0 / 2	
Respiratory failure			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 329 (0.30%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 329 (0.61%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic ulcer			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 329 (0.30%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 329 (0.30%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			

subjects affected / exposed	2 / 329 (0.61%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 329 (0.30%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery embolism			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal infarct			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal embolism			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Osteoarthritis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 329 (0.30%)	3 / 331 (0.91%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 329 (0.30%)	5 / 331 (1.51%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory tract infection			
subjects affected / exposed	0 / 329 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 329 (0.30%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Zinpentraxin Alfa	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 329 (38.91%)	140 / 331 (42.30%)	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	29 / 329 (8.81%)	31 / 331 (9.37%)	
occurrences (all)	55	42	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	14 / 329 (4.26%)	17 / 331 (5.14%)	
occurrences (all)	14	22	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	34 / 329 (10.33%)	35 / 331 (10.57%)	
occurrences (all)	39	48	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	20 / 329 (6.08%)	27 / 331 (8.16%)	
occurrences (all)	22	29	
Cough			
subjects affected / exposed	38 / 329 (11.55%)	42 / 331 (12.69%)	
occurrences (all)	42	46	
Infections and infestations			
COVID-19			
subjects affected / exposed	57 / 329 (17.33%)	57 / 331 (17.22%)	
occurrences (all)	60	59	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2020	This protocol was amended for the following reasons: 1. Changes to the Sponsor, Medical Monitor, PFT parameters; 2. To clarify: that participants with chronic medical issues may be at higher risk for serious illness from COVID-19, that participants who require high-resolution computed tomography (HRCT) scan during screening will have an additional one at Week 52, that reloading of 3 doses of PRM-151 would be required on the resumption of study treatment if a dose was missed, the use of pirfenidone or nintedanib treatment was permitted, that baseline serum concentration would be analyzed for all participants, that body weight should be measured at the start of each dosing period, administration of study drug could be permitted in other settings if participants couldn't attend study site, that precautions are to be taken when performing pulmonary function tests, 6-MW test should be followed by other tests, what events were recorded as health care utilization, blood PAXgene was not applicable for Chinese participants enrolled in mainland China, participants should be followed up by telephone if they couldn't attend the study site, that screening for infections prior to and during the study should be considered during a pandemic, the safety evaluable population, and the number of sites participating in the study; 3. Placebo was included as an IMP; 4.Updates to the permitted and prohibited therapy; 5.The sequence of assessments, pregnancy safety requirements, AE reporting period, efficacy and biomarker analyses were amended; 6. Medical history requirements were updated; 7. Oxygen saturation was included as part of vital sign measurements; 8. An independent, blinded Adjudication Committee was added; 9. SARS-CoV-2 serology testing was added as a lab assessment; 10. Serum sample for tryptase has been added in case of IRRs; 11.Clinically significant ECG abnormalities would be reported as AEs; 12. A statistician was added to the iDMC; 13. Appendices were updated.
13 November 2020	This protocol was amended for the following reasons: 1) PK samples were to be collected as plasma instead of serum; 2) Clarification that lung biopsies should be submitted; 3) Clarification of the formulation of PRM-151; 4) Clarification that clarified that for loading or reloading doses, scheduled efficacy assessments would only be performed on the first of the three loading dose days; 5) Language was added to indicate that acceptability of the spirometry and diffusing capacity for carbon monoxide data was determined by over-readers blinded to study drug treatment; 6) Information regarding acute or suspected acute IPF exacerbation would no longer need to be recorded; 7) Serious hypersensitivity reactions and Grade 4 IRR or two Grade 3 IRRs were added as reasons for permanent study treatment discontinuation; 8) After the end of the AE reporting period, all deaths did not need to be reported on the eCRF; 9) Clarification regarding suspected and unsuspected SAEs reporting; 10) Additional details regarding iDMC reviews were added; 11) Appendices were amended.

28 April 2022	This protocol was amended for the following reasons: 1) Additional text was added throughout the protocol to further clarify or explain information in more detail; 2) "Progression-free survival"was updated to "Time to disease progression" in secondary efficacy objective; 3) Exclusion criteria was updated; 4) Clarification of vital sign measurements at dosing visits; 5) Clarification that all past anti fibrotic therapy would be recorded; 6) Clarification that participants who had high-resolution computed tomography (HRCT) at screening received further HRCT imaging at Week 52; 7) Clarification that medical occurrences that began before the start of study treatment but after obtaining informed consent would be recorded on the electronic case report form (eCRF); 8) Clarification that DLCO assessments would be performed using local equipment; 9) Clarification that oxygen titration procedures would be conducted as per local standard of care; 10) Clarification that blood sample for a serum tryptase sample and complement C3 test would be collected at the time of a suspected anaphylaxis or hypersensitivity event whenever possible; 10) Additional information was provided on sample collection; 11) Assessments following hospitalization for COVID-19 would be collected and analysed; 12) The supplementary estimand was removed; 13) Clarification that an external global Steering Committee provided oversight of Studies WA42293 and WA42294; 14) The international non-proprietary name replaced the RO number throughout the protocol.

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 based on the futility analysis which concluded that zinpentraxin alfa was unlikely to meet its primary endpoint.

Notes: