Clinical trial results:
A Phase 2 Trial to Evaluate the Efficacy of PRM-151 in Subjects with Idiopathic Pulmonary Fibrosis (IPF)

Summary

EudraCT number	2014-004782-24
Trial protocol	DE BE CZ ES HU IT
Global end of trial date	03 April 2019

Results information

Result version number	v1 (current)
This version publication date	10 June 2021
First version publication date	10 June 2021

Trial information

Trial identification

Sponsor protocol code	PRM-151-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02550873
WHO universal trial number (UTN)	-
Other trial identifiers	Promedior, Inc.: PRM-151-202

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	23 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2019
Global end of trial reached?	Yes
Global end of trial date	03 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study randomized period was: determine the effect size of PRM-151 relative to placebo in change from Baseline to Week 28 in mean FVC [% predicted], pooling patients on a stable dose of pirfenidone or nintedanib and patients not on other treatment for IPF.
The objectives of the open-label extension (OLE) were to analyze long-term safety and efficacy of PRM-151 over a 128-week period of exposure (RP + OLE).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki. All patients received information about the study and provided voluntary consent prior to conducting any study-related procedures. All executed originals of the ICFs were retained by the Investigator as part of the site study records. Copies of the signed ICFs were to be given to the patient or patient's legally authorized representative.

Background therapy:

The study population included both patients treated with a stable dose of pirfenidone or nintedanib and patients with no background pirfenidone or nintedanib therapy (either treatment naïve or discontinued prior to enrollment).

Evidence for comparator: -

Actual start date of recruitment	07 September 2015
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	Netherlands: 21
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 73
Worldwide total number of subjects	117
EEA total number of subjects	43

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)	31
From 65 to 84 years	86
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 18 centers in the United States and the European Union.

Pre-assignment

Screening details:

151 patients were screened for the study. Of these, 117 were found to be eligible and were randomized. One patient dropped out of the study prior to receiving any study drug.
111 patients completed the randomized phase (RP) and entered the open-label extension (OLE).

Period 1

Period 1 title	Randomized double-blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

All study personnel, with the exception of the unblinded site pharmacist, were blinded to the treatment allocation to which patients were randomized. This blinding was maintained during the dispensing of investigational product.

Arms

Are arms mutually exclusive?	Yes
Arm title	PRM-151 treatment arm

Arm description:

PRM-151 10 mg/kg IV infusion over 60 minutes days 1, 3, and 5, then one infusion every 4 weeks

Arm type	Experimental
Investigational medicinal product name	PRM-151
Investigational medicinal product code	
Other name	Recombinant human pentraxin 2
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

PRM-151 10 mg/kg IV infusion over 60 minutes days 1, 3, and 5, then one infusion every 4 weeks

Arm title	Placebo arm

Arm description:

Placebo IV infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks

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

Dosage and administration details:

Placebo IV infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks.

Number of subjects in period 1[1]	PRM-151 treatment arm	Placebo arm
Started	77	39
Completed	74	37
Not completed	3	2
Adverse event, serious fatal	-	1
Disease progression	1	1
Adverse event, non-fatal	2	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 151 patients were screened for the study. Of these, 117 were found to be eligible and were randomized. One patient dropped out of the study prior to receiving any study drug, therefore only 116 subjects were included.

Period 2

Period 2 title	Open-label extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ex-Placebo

Arm description:

Patients who entered OLE and received placebo during RP

Arm type	Experimental
Investigational medicinal product name	PRM-151
Investigational medicinal product code	
Other name	Recombinant human pentraxin 2
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients who participated in the OLE received PRM-151 at a dose of 10 mg/kg as an IV infusion over 60 minutes on Days 1, 3, and 5, followed by 1 infusion every 4 weeks. Dosing on Days 1, 3, and 5 was repeated every 28 weeks during the OLE.

Arm title	Ex-Treated

Arm description:

Patients who entered OLE and received PRM-151 during RP

Arm type	Experimental
Investigational medicinal product name	PRM-151
Investigational medicinal product code	
Other name	Recombinant human pentraxin 2
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients who participated in the OLE received PRM-151 at a dose of 10 mg/kg as an IV infusion over 60 minutes on Days 1, 3, and 5, followed by 1 infusion every 4 weeks. Dosing on Days 1, 3, and 5 was repeated every 28 weeks during the OLE.

Number of subjects in period 2	Ex-Placebo	Ex-Treated
Started	37	74
Completed	20	37
Not completed	17	37
Consent withdrawn by subject	3	16
Sponsor's request	1	-
Physician decision	-	1
Adverse event, non-fatal	7	10
Other	1	4
Progression of disease	5	6

Baseline characteristics

Reporting groups	
Reporting group title	PRM-151 treatment arm
Reporting group description:	
PRM-151 10 mg/kg IV infusion over 60 minutes days 1, 3, and 5, then one infusion every 4 weeks	
Reporting group title	Placebo arm
Reporting group description:	
Placebo IV infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks	

Reporting group values	PRM-151 treatment arm	Placebo arm	Total
Number of subjects	77	39	116
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)	20	11	31
From 65-84 years	57	28	85
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	69.03	67.62	
standard deviation	± 6.32	± 7.07	-
Gender categorical Units: Subjects			
Female	12	10	22
Male	65	29	94
Ethnicity/Race Units: Subjects			
Caucasian	74	39	113
Black or African-American	1	0	1
Hispanic	1	0	1
Asian	1	0	1
IPF therapy status at baseline Units: Subjects			
Concurrent IPF therapy (Pirfenidone)	39	22	61
Concurrent IPF therapy (Nintedanib)	22	8	30
No concurrent IPF therapy (IPF therapy naive)	8	7	15
No concurrent IPF therapy (discontinued)	8	2	10
Comorbid conditions (GERD)			

Units: Subjects			
GERD present at baseline	47	16	63
no GERD at baseline	30	23	53
Comorbid conditions (Hypertension) Units: Subjects			
Hypertension present at baseline	38	14	52
No hypertension at baseline	39	25	64
Comorbid conditions (Cardiac disorders) Units: Subjects			
Cardiac disorders present at baseline	29	7	36
No cardiac disorders at baseline	48	32	80
Comorbid conditions (Coronary artery disease) Units: Subjects			
Coronary artery disease present at baseline	12	4	16
No coronary artery disease at baseline	65	35	100
Weight Units: kg			
arithmetic mean	86.1	87.5	
standard deviation	± 15.2	± 13.4	-
Time since diagnosis of IPF Units: years			
arithmetic mean	3.7	3.9	
standard deviation	± 2.2	± 2.6	-
FVC Units: mL			
arithmetic mean	2733	2763	
standard deviation	± 630	± 654	-
FEV1/FVC Units: percent			
arithmetic mean	81.2	81.6	
standard deviation	± 5.1	± 4.7	-
Hemoglobin-corrected DLCO Units: percentage of predicted values			
arithmetic mean	40.1	43.2	
standard deviation	± 9.1	± 10.5	-
6MWD Units: meters			
arithmetic mean	434.8	457.7	
standard deviation	± 92.5	± 117.7	-
SpO2 at rest Units: percentage			
arithmetic mean	95.6	95.5	
standard deviation	± 2.1	± 1.8	-
Baseline pentraxin 2 concentrations Units: ng/mL			
arithmetic mean	30456.17	30961.54	
standard deviation	± 13566.81	± 10090.47	-

Subject analysis sets	
Subject analysis set title	Placebo No Background Therapy
Subject analysis set type	Sub-group analysis
Subject analysis set description: No background therapy placebo group	
Subject analysis set title	PRM-151 No Background Therapy
Subject analysis set type	Sub-group analysis
Subject analysis set description: No Background Therapy PRM-151 10 mg/kg IV group	
Subject analysis set title	Placebo Pirfenidone or Nintendanib
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pirfenidone or Nintendanib Placebo group	
Subject analysis set title	PRM-151 Pirfenidone or Nintendanib
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pirfenidone or Nintendanib PRM-151 10 mg/kg IV group	

Reporting group values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib
Number of subjects	9	16	30
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)			
From 65-84 years			
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			
Male			
Ethnicity/Race Units: Subjects			
Caucasian			
Black or African-American			
Hispanic			
Asian			
IPF therapy status at baseline Units: Subjects			
Concurrent IPF therapy (Pirfenidone)			

Concurrent IPF therapy (Nintedanib) No concurrent IPF therapy (IPF therapy naive) No concurrent IPF therapy (discontinued)			
Comorbid conditions (GERD) Units: Subjects			
GERD present at baseline no GERD at baseline			
Comorbid conditions (Hypertension) Units: Subjects			
Hypertension present at baseline No hypertension at baseline			
Comorbid conditions (Cardiac disorders) Units: Subjects			
Cardiac disorders present at baseline No cardiac disorders at baseline			
Comorbid conditions (Coronary artery disease) Units: Subjects			
Coronary artery disease present at baseline No coronary artery disease at baseline			
Weight Units: kg arithmetic mean standard deviation	±	±	±
Time since diagnosis of IPF Units: years arithmetic mean standard deviation	±	±	±
FVC Units: mL arithmetic mean standard deviation	±	±	±
FEV1/FVC Units: percent arithmetic mean standard deviation	±	±	±
Hemoglobin-corrected DLCO Units: percentage of predicted values arithmetic mean standard deviation	±	±	±
6MWD Units: meters arithmetic mean standard deviation	±	±	±
SpO2 at rest Units: percentage arithmetic mean standard deviation	±	±	±

Baseline pentraxin 2 concentrations Units: ng/mL arithmetic mean standard deviation	±	±	±

Reporting group values	PRM-151 Pirfenidone or Nintendanib		
Number of subjects	61		
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)			
From 65-84 years			
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female			
Male			
Ethnicity/Race Units: Subjects			
Caucasian			
Black or African-American			
Hispanic			
Asian			
IPF therapy status at baseline Units: Subjects			
Concurrent IPF therapy (Pirfenidone)			
Concurrent IPF therapy (Nintedanib)			
No concurrent IPF therapy (IPF therapy naive)			
No concurrent IPF therapy (discontinued)			
Comorbid conditions (GERD) Units: Subjects			
GERD present at baseline			
no GERD at baseline			
Comorbid conditions (Hypertension) Units: Subjects			
Hypertension present at baseline			
No hypertension at baseline			
Comorbid conditions (Cardiac disorders)			

Units: Subjects			
Cardiac disorders present at baseline No cardiac disorders at baseline			
Comorbid conditions (Coronary artery disease) Units: Subjects			
Coronary artery disease present at baseline No coronary artery disease at baseline			
Weight Units: kg arithmetic mean standard deviation	±		
Time since diagnosis of IPF Units: years arithmetic mean standard deviation	±		
FVC Units: mL arithmetic mean standard deviation	±		
FEV1/FVC Units: percent arithmetic mean standard deviation	±		
Hemoglobin-corrected DLCO Units: percentage of predicted values arithmetic mean standard deviation	±		
6MWD Units: meters arithmetic mean standard deviation	±		
SpO2 at rest Units: percentage arithmetic mean standard deviation	±		
Baseline pentraxin 2 concentrations Units: ng/mL arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	PRM-151 treatment arm
Reporting group description: PRM-151 10 mg/kg IV infusion over 60 minutes days 1, 3, and 5, then one infusion every 4 weeks	
Reporting group title	Placebo arm
Reporting group description: Placebo IV infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks	
Reporting group title	Ex-Placebo
Reporting group description: Patients who entered OLE and received placebo during RP	
Reporting group title	Ex-Treated
Reporting group description: Patients who entered OLE and received PRM-151 during RP	
Subject analysis set title	Placebo No Background Therapy
Subject analysis set type	Sub-group analysis
Subject analysis set description: No background therapy placebo group	
Subject analysis set title	PRM-151 No Background Therapy
Subject analysis set type	Sub-group analysis
Subject analysis set description: No Background Therapy PRM-151 10 mg/kg IV group	
Subject analysis set title	Placebo Pirfenidone or Nintendanib
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pirfenidone or Nintendanib Placebo group	
Subject analysis set title	PRM-151 Pirfenidone or Nintendanib
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pirfenidone or Nintendanib PRM-151 10 mg/kg IV group	

Primary: Change from Baseline to Week 28 in mean FVC [% predicted]

End point title	Change from Baseline to Week 28 in mean FVC [% predicted]
End point description: Determine the effect size of PRM-151 relative to placebo in change from Baseline to Week 28 in mean FVC% predicted, pooling subjects on a stable dose of pirfenidone or nintedanib with subjects not on other treatment for IPF.	
End point type	Primary
End point timeframe: Baseline to 28 week	

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Percentage of predicted FVC				
arithmetic mean (standard error)	-2.5 (± 0.42)	-4.8 (± 0.58)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Primary analysis was conducted on the All Treated Set (ATS) population (all randomized patients having received at least one administration of the study medication, allocated as randomized for analysis). The following statistical hypotheses were tested:
• H0: Absence of difference between the treatment groups.
• H1: A difference exists between the treatment groups.

Comparison groups	PRM-151 treatment arm v Placebo arm
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.1
upper limit	3.5
Variability estimate	Standard error of the mean
Dispersion value	0.72

Secondary: Change in 6-minute walk distance

End point title	Change in 6-minute walk distance

End point description:

Determine the effect size of PRM-151 relative to placebo on 6-minute walk distance (6MWD).

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: meters				
arithmetic mean (standard error)	-0.5 (± 4.92)	-31.8 (± 6.83)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	PRM-151 treatment arm v Placebo arm
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	31.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	17.4
upper limit	45.1
Variability estimate	Standard error of the mean
Dispersion value	8.42

Secondary: Change in total lung volume on HRCT

End point title	Change in total lung volume on HRCT
End point description:	
Mean change from Baseline to Week 28 in total lung volume, using quantitative imaging software, all treated set	
End point type	Secondary
End point timeframe:	
Baseline to Week 28	

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	14	26	52
Units: mililiters				
arithmetic mean (standard error)	-197.3 (± 86.66)	-103.8 (± 78.46)	-201.6 (± 62.41)	-108.1 (± 45.85)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
All patients from the ATS population who had HRCT data at both the Baseline and Week 28 time points	
Comparison groups	PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib v Placebo No Background Therapy
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2032
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	93.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-27.7
upper limit	214.7
Variability estimate	Standard error of the mean
Dispersion value	72.98

Secondary: Change in volume of parenchymal features on HRCT (%), representative of ILA

End point title	Change in volume of parenchymal features on HRCT (%), representative of ILA
End point description:	
Mean change from Baseline to Week 28 in volume of parenchymal features on HRCT (in % of total lung volume) representative of interstitial lung abnormalities (ILA) including ground glass density, reticular changes, and honeycombing, using quantitative imaging software.	
End point type	Secondary
End point timeframe:	
Baseline to Week 28	

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	14	26	52
Units: percentage				
arithmetic mean (standard error)	1.5 (± 2.33)	2.6 (± 2.10)	1.9 (± 1.68)	3.0 (± 1.23)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5835
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.2
upper limit	4.3
Variability estimate	Standard error of the mean
Dispersion value	1.96

Secondary: Change in volume of parenchymal features on HRCT (ml), representative of ILA

End point title	Change in volume of parenchymal features on HRCT (ml), representative of ILA

End point description:

Mean change from Baseline to Week 28 in volume of parenchymal features on HRCT (in ml) representative of interstitial lung abnormalities (ILA) including ground glass density, reticular changes, and honeycombing, using quantitative imaging software.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	14	26	52
Units: mililiters				
arithmetic mean (standard error)	17.8 (± 55.26)	49.7 (± 49.65)	49.0 (± 39.64)	80.9 (± 29.21)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4927
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	31.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-45
upper limit	108.8
Variability estimate	Standard error of the mean
Dispersion value	46.33

Secondary: Change from in volume of parenchymal features on HRCT (in %) non-ILA

End point title	Change from in volume of parenchymal features on HRCT (in %) non-ILA

End point description:

Mean change from Baseline to Week 28 in volume of parenchymal features on HRCT (in % of total lung volume) representative of normal lung (non-ILA), including normal and mild low attenuation areas, using quantitative imaging software.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	14	26	52
Units: Percentage of total lung volume				
arithmetic mean (standard error)	-1.4 (± 2.27)	-2.6 (± 2.05)	-2.1 (± 1.64)	-3.3 (± 1.20)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5196
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.4
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	1.91

Secondary: Change in volume of parenchymal features on HRCT (ml), non-ILA

End point title	Change in volume of parenchymal features on HRCT (ml), non-ILA

End point description:

Mean change from Baseline to Week 28 in volume of parenchymal features on HRCT (in ml) representative of normal lung (non-ILA), including normal and mild low attenuation areas, using quantitative imaging software.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	14	26	52
Units: mililiters				
arithmetic mean (standard error)	-208.8 (± 121.20)	-165.2 (± 109.58)	-244.7 (± 87.45)	-201.1 (± 64.16)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6707
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	43.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-126.3
upper limit	213.5
Variability estimate	Standard error of the mean
Dispersion value	102.28

Secondary: Correlation between Change from Baseline to Week 28 in FVC (%) and Change from Baseline to Week 28 in Total Lung Volume (mL)

End point title	Correlation between Change from Baseline to Week 28 in FVC (%) and Change from Baseline to Week 28 in Total Lung Volume (mL)

End point description:

Correlation between mean change from Baseline to Week 28 in FVC [% predicted] and mean change from Baseline to Week 28 in total lung volume (in ml) representative of interstitial lung abnormalities (ILA), including ground glass density, reticular changes, and honeycombing by quantitative imaging software.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	33		
Units: Correlation coefficient				
number (confidence interval 95%)	0.3776 (0.1337 to 0.5741)	0.6788 (0.4288 to 0.8256)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	PRM-151 treatment arm v Placebo arm
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	Clopper-Pearson

Notes:

[1] - correlation analysis

Secondary: Correlation between Change from Baseline to Week 28 in FVC (%) and Change from Baseline to Week 28 in Interstitial Lung Abnormalities (mL)

End point title	Correlation between Change from Baseline to Week 28 in FVC (%) and Change from Baseline to Week 28 in Interstitial Lung Abnormalities (mL)

End point description:

Correlation between mean change from Baseline to Week 28 in FVC [% predicted] and mean change from Baseline to Week 28 in volume of parenchymal features on HRCT (in % of total lung volume) representative of interstitial lung abnormalities (ILA), including ground glass density, reticular changes, and honeycombing by quantitative imaging software.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	33		
Units: Correlation coefficient				
number (confidence interval 95%)	-0.5027 (-0.6686 to -0.2812)	-0.4570 (-0.6880 to -0.1279)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	PRM-151 treatment arm v Placebo arm

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	Clopper-Pearson

Notes:

[2] - Correlation analysis

Secondary: Proportion of subjects with a decline in FVC [% predicted] of ≥ 5% and ≥10% from baseline to week 28

End point title	Proportion of subjects with a decline in FVC [% predicted] of ≥ 5% and ≥10% from baseline to week 28

End point description:

Pulmonary Function Tests for the proportion (%) of subjects with a decline in FVC [% predicted] of ≥5% and ≥10% from baseline to week 28

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)				
Decline in % Predicted FVC ≥ 5%	2	2	11	18
Decline in % Predicted FVC ≥ 10%	0	1	3	1

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

for decline in % Predicted FVC ≥ 5%

Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4179 [3]
Method	Mixed models analysis

Notes:

[3] - for decline in % Predicted FVC ≥ 5%

Statistical analysis title	Statistical analysis 2

Statistical analysis description: for decline in % predicted FVC ≥ 10%	
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2184 [4]
Method	Mixed models analysis

Notes:

[4] - for decline in % predicted FVC ≥ 10%

Secondary: Proportion of subjects with a decline in FVC [ml] of ≥ 100ml and ≥ 200ml from baseline to week 28.

End point title	Proportion of subjects with a decline in FVC [ml] of ≥ 100ml and ≥ 200ml from baseline to week 28.

End point description:

Pulmonary Function Tests for the Proportion (%) of subjects with a decline in FVC [ml] of ≥ 100ml and ≥ 200ml from baseline to week 28.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)				
Decline in FVC ≥100 mL	2	5	16	32
Decline in FVC ≥200 mL	1	2	8	19

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: for decline in FVC ≥ 100 mL	
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5976 [5]
Method	Mixed models analysis

Notes:

[5] - for decline in FVC ≥ 100 mL

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

for decline in FVC ≥ 200 mL

Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5976 [6]
Method	Mixed models analysis

Notes:

[6] - for decline in FVC ≥ 200 mL

Secondary: Proportion of subjects with an increase in FVC [% predicted] of ≥ 5% and ≥ 10% from baseline to week 28

End point title	Proportion of subjects with an increase in FVC [% predicted] of ≥ 5% and ≥ 10% from baseline to week 28

End point description:

Pulmonary Function Tests for the Proportion (%) of subjects with an increase in FVC [% predicted] of ≥5% and ≥ 10% from baseline to week 28.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)				
Increase in % Predicted FVC ≥5%	0	1	0	1
Increase in % Predicted FVC ≥10%	0	0	0	0

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description: for increase in % predicted FVC ≥ 5%	
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2912 [7]
Method	Mixed models analysis

Notes:

[7] - for increase in % predicted FVC ≥ 5%

Secondary: Proportion of subjects with an increase in FVC [ml] of ≥ 100 ml and ≥ 200 ml from baseline to week 28

End point title	Proportion of subjects with an increase in FVC [ml] of ≥ 100 ml and ≥ 200 ml from baseline to week 28

End point description:

Pulmonary Function Tests for the Proportion of subjects with an increase in FVC [ml] of ≥ 100 ml and ≥200 ml from baseline to week 28

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)				
Increase in FVC ≥100 mL	0	1	0	6
Increase in FVC ≥200 mL	0	0	0	0

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

for increase in FVC ≥ 100 mL

Comparison groups	PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib v Placebo No Background Therapy

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0508 [8]
Method	Mixed models analysis

Notes:

[8] - for increase in FVC ≥ 100 mL

Secondary: Proportion of subjects with stable disease by FVC [% predicted], defined as a change in FVC [% predicted] of < 5% from baseline to week 28

End point title	Proportion of subjects with stable disease by FVC [% predicted], defined as a change in FVC [% predicted] of < 5% from baseline to week 28

End point description:

Pulmonary Function Tests for the Proportion of subjects with stable disease by FVC [% predicted], defined as a change in FVC [% predicted] of < 5% from baseline to week 28.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)	6	10	16	35

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6308
Method	Mixed models analysis

Secondary: Proportion of subjects with stable disease by FVC in ml, defined as a change in FVC of < 100ml from Baseline to week 28

End point title	Proportion of subjects with stable disease by FVC in ml, defined as a change in FVC of < 100ml from Baseline to week 28

End point description:

Pulmonary function tests for the Proportion of subjects with stable disease by FVC in ml, defined as a

change in FVC of < 100ml from Baseline to week 28.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	13	27	54
Units: Subjects				
number (not applicable)	6	7	11	16

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo No Background Therapy v PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1846
Method	Mixed models analysis

Secondary: Change in % predicted Hb-corrected DLCO

End point title	Change in % predicted Hb-corrected DLCO

End point description:

Mean change from Baseline to Week 28 in Hb-corrected DLCO i.e., diffusion capacity of carbon monoxide [% predicted].

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	Placebo No Background Therapy	PRM-151 No Background Therapy	Placebo Pirfenidone or Nintendanib	PRM-151 Pirfenidone or Nintendanib
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	16	30	61
Units: Percentage				
arithmetic mean (standard error)	-2.4 (± 1.60)	-2.8 (± 1.39)	-2.5 (± 1.10)	-3.0 (± 0.84)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	PRM-151 No Background Therapy v Placebo Pirfenidone or Nintendanib v Placebo No Background Therapy v PRM-151 Pirfenidone or Nintendanib
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7424
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.6
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	1.31

Secondary: The Incidence of TEAEs	
End point title	The Incidence of TEAEs
End point description: Any Treatment-Emergent Adverse Event (TEAE), SAF population	
End point type	Secondary
End point timeframe: Baseline to Week 28	

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	71	36		

Statistical analyses

No statistical analyses for this end point

Secondary: The Incidence of TESAEs

End point title	The Incidence of TESAEs
End point description: Serious TEAEs, SAF population	
End point type	Secondary
End point timeframe: Baseline to Week 28	

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	6	4		

Statistical analyses

No statistical analyses for this end point

Secondary: The Incidence of Respiratory Decline TEAEs

End point title	The Incidence of Respiratory Decline TEAEs
End point description: Incidence of respiratory TEAEs, SAF population "Respiratory decline" events are defined as follows: - Unscheduled visits to a healthcare professional for respiratory status deterioration. - Urgent care visit for respiratory status deterioration. - Hospitalization due to a worsening or exacerbation of respiratory symptoms.	
End point type	Secondary
End point timeframe: Baseline to Week 28	

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	11	4		

Statistical analyses

No statistical analyses for this end point

Secondary: The Incidence of Respiratory Decline TESAEs

End point title	The Incidence of Respiratory Decline TESAEs

End point description:

Incidence of respiratory serious TEAEs, SAF population
"Respiratory decline" events are defined as follows:
- Unscheduled visits to a healthcare professional for respiratory status deterioration.
- Urgent care visit for respiratory status deterioration.
- Hospitalization due to a worsening or exacerbation of respiratory symptoms.

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of subjects discontinuing study drug due to TEAEs

End point title	The proportion of subjects discontinuing study drug due to TEAEs

End point description:

TEAEs Leading to Permanent Discontinuation of Study Drug

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: All cause mortality

End point title	All cause mortality

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality due to respiratory deterioration

End point title	Mortality due to respiratory deterioration

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 28

End point values	PRM-151 treatment arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	39		
Units: Subjects				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in FVC (% predicted) - OLE

End point title	Change in FVC (% predicted) - OLE

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline to Week 52 (OLE)

End point values	Ex-Placebo	Ex-Treated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	74		
Units: Percentage of predicted FVC				
arithmetic mean (standard error)	-5.0 (± 0.48)	-3.7 (± 0.34)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Ex-Placebo v Ex-Treated
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0199
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	0.59

Other pre-specified: Change in FVC (ml) - OLE

End point title	Change in FVC (ml) - OLE

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline to Week 52 (OLE)

End point values	Ex-Placebo	Ex-Treated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	74		
Units: mililiters				
arithmetic mean (standard error)	-229.5 (± 19.42)	-179.9 (± 13.64)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Ex-Treated v Ex-Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0365
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	49.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.6
upper limit	88.7
Variability estimate	Standard error of the mean
Dispersion value	23.73

Other pre-specified: Change in 6-minute walk distance (OLE)

End point title	Change in 6-minute walk distance (OLE)
End point description:	
End point type	Other pre-specified
End point timeframe:	
Baseline to Week 52 (OLE)	

End point values	Ex-Placebo	Ex-Treated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	74		
Units: meters				
arithmetic mean (standard error)	-29.0 (± 5.74)	-10.6 (± 4.09)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Ex-Placebo v Ex-Treated
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0089
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	18.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.9
upper limit	30.1
Variability estimate	Standard error of the mean
Dispersion value	7.05

Other pre-specified: Number of subjects with adverse events emerging during the OLE

End point title	Number of subjects with adverse events emerging during the OLE

End point description:

Number of subjects with Treatment-Emergent Adverse Events Emerging During the Open-Label Extension up to and Including Week 128 (SAF-OLE Population)

End point type	Other pre-specified

End point timeframe:

After the first dose in the OLE and through Week 128

End point values	Ex-Placebo	Ex-Treated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	74		
Units: Subjects				
Any TEAE	36	69		
Any TEAE leading to permanent study drug discontin	10	18		
Any TEAE leading to permanent study discontinuatio	7	10		
Any TEAE leading to hospitalization	13	25		
Any mild TEAE	31	65		
Any moderate TEAE	28	53		
Any severe TEAE	8	23		
Any life-threatening TEAE	2	1		
Any TEAE possibly or probably related to study dru	14	24		
Any infusion-related reaction TEAE	3	7		
Any respiratory decline TEAE	8	31		

Any TEAE in the HLT of Liver Function Analyses	1	2		
Any TEAE in the SOC of Renal and urinary disorders	4	9		
Any IPF exacerbations reported as TEAEs	1	6		
Any serious TEAE	15	32		
Any mild serious TEAE	1	1		
Any moderate serious TEAE	6	10		
Any severe serious TEAE	7	20		
Any life-threatening serious TEAE	2	1		
Death	4	10		
Any serious TEAE leading to permanent study drug d	10	14		
Any serious TEAE leading to permanent study discon	6	7		
Any serious TEAE leading to hospitalization	13	25		
Any serious TEAE possibly or probably related to s	1	1		
Any infusion-related reaction serious TEAE	0	1		
Any respiratory decline serious TEAE	6	16		
Any serious TEAE in the HLT of Liver Function Anal	0	0		
Any serious TEAE in the SOC of Renal and urinary d	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

RP - 28 weeks
OLE - TEAEs occurring after the first dose in the OLE and through Week 128 are included.

Adverse event reporting additional description:

RP - All AEs from signing of informed consent until last study visit were entered in the database, but only AEs from the time of first study treatment dose administered to the patient (TEAEs) until last study visit were analysed.
OLE - TEAEs occurring after the first dose in the OLE and through Week 128 are included.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	PRM-151 treatment arm (RP)

Reporting group description:

PRM-151 10 mg/kg IV infusion over 60 minutes days 1, 3, and 5, then one infusion every 4 weeks

Reporting group title	Placebo arm (RP)

Reporting group description:

Placebo IV infusion over 60 minutes on days 1, 3, and 5, then one infusion every 4 weeks

Reporting group title	Ex-placebo (OLE)

Reporting group description: -

Reporting group title	Ex-treated (OLE)

Reporting group description: -

Serious adverse events	PRM-151 treatment arm (RP)	Placebo arm (RP)	Ex-placebo (OLE)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 77 (7.79%)	4 / 39 (10.26%)	15 / 37 (40.54%)
number of deaths (all causes)	0	1	6
number of deaths resulting from adverse events	0	1	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma metastatic			

subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma stage I			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer extensive stage			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Surgical and medical procedures			

Alcohol detoxification			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung transplant			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	1 / 77 (1.30%)	0 / 39 (0.00%)	0 / 37 (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
Idiopathic Pulmonary Fibrosis			
subjects affected / exposed	1 / 77 (1.30%)	2 / 39 (5.13%)	3 / 37 (8.11%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 4
Dyspnoea			
subjects affected / exposed	0 / 77 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Acute respiratory failure			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumomediastinum			

subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Transplant evaluation			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary Artery Disease			

subjects affected / exposed	1 / 77 (1.30%)	0 / 39 (0.00%)	0 / 37 (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
Cardiomyopathy			
subjects affected / exposed	1 / 77 (1.30%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 77 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Myocardial infarction			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia supraventricular			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Embolic Cerebral Infarction			
subjects affected / exposed	1 / 77 (1.30%)	0 / 39 (0.00%)	0 / 37 (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
Dysgeusia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Tendonitis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 77 (0.00%)	1 / 39 (2.56%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 77 (1.30%)	0 / 39 (0.00%)	0 / 37 (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
Respiratory Tract Infection			
subjects affected / exposed	0 / 77 (0.00%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Influenza			
subjects affected / exposed	0 / 77 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Lung infection			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ex-treated (OLE)		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 74 (43.24%)		
number of deaths (all causes)	10		
number of deaths resulting from adverse events	10		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma metastatic			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma stage I			

subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to lymph nodes				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer extensive stage				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the tongue				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Carotid artery stenosis				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Alcohol detoxification				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Lung transplant				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	2 / 74 (2.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary Embolism				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Idiopathic Pulmonary Fibrosis				
subjects affected / exposed	8 / 74 (10.81%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 4			
Dyspnoea				
subjects affected / exposed	2 / 74 (2.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	2 / 74 (2.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumomediastinum				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				

subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Depression				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Transplant evaluation				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Rib fracture				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary Artery Disease				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				

subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial Fibrillation				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 74 (2.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Acute coronary syndrome				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arrhythmia supraventricular				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				

subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Embolic Cerebral Infarction			
subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysgeusia			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Tendonitis			

subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	5 / 74 (6.76%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 2			
Lower Respiratory Tract Infection				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 74 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metapneumovirus infection			
subjects affected / exposed	0 / 74 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PRM-151 treatment arm (RP)	Placebo arm (RP)	Ex-placebo (OLE)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 77 (92.21%)	36 / 39 (92.31%)	36 / 37 (97.30%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	3
Blood pressure fluctuation			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 77 (14.29%)	3 / 39 (7.69%)	1 / 37 (2.70%)
occurrences (all)	15	6	1
Dizziness			
subjects affected / exposed	6 / 77 (7.79%)	3 / 39 (7.69%)	2 / 37 (5.41%)
occurrences (all)	7	4	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 77 (16.88%)	4 / 39 (10.26%)	5 / 37 (13.51%)
occurrences (all)	20	4	5

Oedema peripheral			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	4
Pyrexia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 77 (11.69%)	2 / 39 (5.13%)	2 / 37 (5.41%)
occurrences (all)	11	2	2
Nausea			
subjects affected / exposed	5 / 77 (6.49%)	2 / 39 (5.13%)	1 / 37 (2.70%)
occurrences (all)	6	2	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 77 (18.18%)	2 / 39 (5.13%)	14 / 37 (37.84%)
occurrences (all)	16	2	26
Idiopathic pulmonary fibrosis			
subjects affected / exposed	11 / 77 (14.29%)	5 / 39 (12.82%)	11 / 37 (29.73%)
occurrences (all)	11	6	18
Dyspnoea			
subjects affected / exposed	7 / 77 (9.09%)	4 / 39 (10.26%)	6 / 37 (16.22%)
occurrences (all)	8	4	11
Productive cough			
subjects affected / exposed	3 / 77 (3.90%)	3 / 39 (7.69%)	1 / 37 (2.70%)
occurrences (all)	3	3	1
Hypoxia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	5 / 37 (13.51%)
occurrences (all)	0	0	7
Pulmonary hypertension			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	6
Dyspnoea exertional			

subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	4 / 77 (5.19%)	3 / 39 (7.69%)	2 / 37 (5.41%)
occurrences (all)	5	4	3
Back pain			
subjects affected / exposed	3 / 77 (3.90%)	4 / 39 (10.26%)	3 / 37 (8.11%)
occurrences (all)	3	8	3
Arthralgia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 77 (15.58%)	9 / 39 (23.08%)	5 / 37 (13.51%)
occurrences (all)	15	13	8
Bronchitis			
subjects affected / exposed	8 / 77 (10.39%)	5 / 39 (12.82%)	8 / 37 (21.62%)
occurrences (all)	8	5	10
Upper respiratory tract infection			
subjects affected / exposed	7 / 77 (9.09%)	5 / 39 (12.82%)	8 / 37 (21.62%)
occurrences (all)	7	5	11
Respiratory tract infection			
subjects affected / exposed	4 / 77 (5.19%)	2 / 39 (5.13%)	2 / 37 (5.41%)
occurrences (all)	5	2	3
Sinusitis			
subjects affected / exposed	3 / 77 (3.90%)	3 / 39 (7.69%)	3 / 37 (8.11%)
occurrences (all)	3	4	3
Influenza			
subjects affected / exposed	3 / 77 (3.90%)	3 / 39 (7.69%)	2 / 37 (5.41%)
occurrences (all)	3	3	2
Pneumonia			

subjects affected / exposed	0 / 77 (0.00%)	0 / 39 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 77 (5.19%)	2 / 39 (5.13%)	0 / 37 (0.00%)
occurrences (all)	4	2	0

Non-serious adverse events	Ex-treated (OLE)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 74 (93.24%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	9		
Blood pressure fluctuation			
subjects affected / exposed	4 / 74 (5.41%)		
occurrences (all)	6		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	7		
Dizziness			
subjects affected / exposed	10 / 74 (13.51%)		
occurrences (all)	13		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 74 (18.92%)		
occurrences (all)	18		
Oedema peripheral			
subjects affected / exposed	3 / 74 (4.05%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	3 / 74 (4.05%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	15 / 74 (20.27%)		
occurrences (all)	26		
Nausea			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	8		
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 74 (21.62%)		
occurrences (all)	22		
Idiopathic pulmonary fibrosis			
subjects affected / exposed	22 / 74 (29.73%)		
occurrences (all)	34		
Dyspnoea			
subjects affected / exposed	26 / 74 (35.14%)		
occurrences (all)	34		
Productive cough			
subjects affected / exposed	9 / 74 (12.16%)		
occurrences (all)	10		
Hypoxia			
subjects affected / exposed	11 / 74 (14.86%)		
occurrences (all)	12		
Pulmonary hypertension			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	8		
Dyspnoea exertional			
subjects affected / exposed	8 / 74 (10.81%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 74 (9.46%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			

Pain in extremity subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 4		
Back pain subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 8		
Arthralgia subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 16		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	13 / 74 (17.57%) 24		
Bronchitis subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 9		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	18 / 74 (24.32%) 21		
Respiratory tract infection subjects affected / exposed occurrences (all)	9 / 74 (12.16%) 11		
Sinusitis subjects affected / exposed occurrences (all)	3 / 74 (4.05%) 3		
Influenza subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 4		
Pneumonia subjects affected / exposed occurrences (all)	9 / 74 (12.16%) 10		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2016	1)Clarification regarding WOCBP birth control 2) Addition of inclusion criterion re lung transplantation 3) Clarification of inclusion criterion re background treatment 4) revision of inclusion criterion re 6MWT 5)Revision of exclusion criterion re immuno-suppressants 6) Exclusion criterion re pregnant/lactating patient 7)Addition to Schedule of Events 8)Change in infusion time 9) Addition to Study Procedures
03 March 2016	minor updates

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.

Sample size was not appropriate to explore additional hypotheses beyond the prespecified primary analyses; diagnosis of IPF is allowing for "possible usual interstitial pneumonia"; HRCT was not centrally read; HRCT susceptible to potential artifacts;

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29800034

http://www.ncbi.nlm.nih.gov/pubmed/31122893