



Clinical trial results:

A Multi-Site, Open-Label Extension Trial of Oral RPC1063 in Relapsing Multiple Sclerosis

Summary

EudraCT number	2015-002500-91
Trial protocol	HU BE GB ES BG SK GR PL LV EE LT PT SE HR IT
Global end of trial date	05 January 2023

Results information

Result version number	v1 (current)
This version publication date	28 December 2023
First version publication date	28 December 2023

Trial information

Trial identification

Sponsor protocol code	RPC01-3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02576717
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	30 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the long-term safety and tolerability of RPC1063 in patients with relapsing multiple sclerosis

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 October 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	Belarus: 203
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Bosnia and Herzegovina: 16
Country: Number of subjects enrolled	Bulgaria: 43
Country: Number of subjects enrolled	Croatia: 32
Country: Number of subjects enrolled	Estonia: 10
Country: Number of subjects enrolled	Georgia: 82
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	Moldova, Republic of: 12
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Poland: 676
Country: Number of subjects enrolled	Portugal: 23
Country: Number of subjects enrolled	Romania: 57
Country: Number of subjects enrolled	Russian Federation: 364
Country: Number of subjects enrolled	Serbia: 177

Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Spain: 57
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Ukraine: 538
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 81
Worldwide total number of subjects	2494
EEA total number of subjects	988

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)	2494
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants must have participated in Trial RPC01-201, Trial RPC01-301, and/or Trial RPC01-1001 prior to joining RPC01-3001.

Pre-assignment

Screening details:

Participants were Pooled According to Treatment Group Assignment in Parent Trial.

Period 1

Period 1 title	Treatment Period: Safety Population (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Parent Treatment Group IFN-B-1a 30 ug

Arm description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Arm type	Experimental
Investigational medicinal product name	RPC1063
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 mg daily by mouth

Arm title	Parent Treatment Group: RPC1063 0.5 mg
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Arm description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Arm type	Experimental
Investigational medicinal product name	RPC1063
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 mg daily by mouth

Arm title	Parent Treatment Group: RPC1063 1.0 mg
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Arm description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Arm type	Experimental
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Investigational medicinal product name	RPC1063
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 mg daily by mouth

Number of subjects in period 1	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg
Started	736	877	881
Transferred from IFN β -1a	0 ^[1]	3 ^[2]	1 ^[3]
Transferred from RPC1063 0.5 mg	0 ^[4]	0 ^[5]	1 ^[6]
From equivalent Placebo group	0 ^[7]	37 ^[8]	35 ^[9]
Completed	562	692	696
Not completed	174	185	185
Adverse event, serious fatal	3	5	3
Physician decision	3	8	9
Covid-19 Pandemic	-	1	1
Adverse event, non-fatal	26	32	26
Other Reasons	14	18	16
Sponsor Decision	-	-	1
Lost to follow-up	9	10	19
Participant Voluntarily Withdrew from Study	91	83	85
Lack of efficacy	24	28	20
Protocol deviation	4	-	5

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: Participants did not transfer from another group.

[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: Participants did not transfer from another group.

[3] - 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: Participants transferred from another group.

[4] - 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: Participants did not transfer from another group.

[5] - 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: Participants transferred from another group.

[6] - 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: Participants transferred from another group.

[7] - 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: Participants did not transfer from another group.

[8] - 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: Participants transferred from another group.

[9] - 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: Participants transferred from another group.

Baseline characteristics

Reporting groups

Reporting group title	Parent Treatment Group IFN-B-1a 30 ug
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: RPC1063 0.5 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: RPC1063 1.0 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg
Number of subjects	736	877	881
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	736	877	881
>=65 years	0	0	0
Sex: Female, Male Units: Participants			
Female	498	595	575
Male	238	282	306
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	8	16
Not Hispanic or Latino	733	869	865
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race Units: Subjects			
White	734	865	875
Black or African American	1	7	6
Asian	0	3	0
Other	1	2	0

Reporting group values	Total		
Number of subjects	2494		

Age Categorical			
Units: Participants			
<=18 years	0		
Between 18 and 65 years	2494		
>=65 years	0		
Sex: Female, Male			
Units: Participants			
Female	1668		
Male	826		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	27		
Not Hispanic or Latino	2467		
Unknown or Not Reported	0		
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	2474		
Black or African American	14		
Asian	3		
Other	3		

End points

End points reporting groups

Reporting group title	Parent Treatment Group IFN-B-1a 30 ug
Reporting group description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Reporting group title	Parent Treatment Group: RPC1063 0.5 mg
Reporting group description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Reporting group title	Parent Treatment Group: RPC1063 1.0 mg
Reporting group description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Parent Treatment Group IFN-B-1a 30 ug ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Parent Treatment Group: RPC1063 0.5 mg ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Parent Treatment Group: RPC1063 1.0 mg ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Withdrawal Analysis Combination
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Parent Treatment Group: Placebo for RPC1063 0.5 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a 7-day titration regimen of RPC1063 to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.	
Subject analysis set title	Parent Treatment Group: Placebo for RPC1063 1 mg

Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Participants received a 7-day titration regimen of RPC1063 to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Primary: Number of Participants Experiencing Adverse Events (AEs)

End point title	Number of Participants Experiencing Adverse Events (AEs) ^[1]
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End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of medicinal product, whether or not considered related to the investigational medicinal product.

End point type	Primary
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End point timeframe:

From first dose to 90-days post last dose (an average of 65 months up to a max of 85 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants	668	775	776	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing Serious Adverse Events (SAEs)

End point title	Number of Participants Experiencing Serious Adverse Events (SAEs) ^[2]
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End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose results in death, is life-threatening (defined as an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe), requires inpatient hospitalization or causes prolongation of existing hospitalization.

End point type	Primary
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End point timeframe:

From first dose to 90-days post last dose (an average of 65 months up to a max of 85 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants	108	139	134	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing Adverse Events (AEs) Leading to Discontinuation

End point title	Number of Participants Experiencing Adverse Events (AEs) Leading to Discontinuation ^[3]
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End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of medicinal product, whether or not considered related to the investigational medicinal product.

End point type	Primary
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End point timeframe:

From first dose to 90-days post last dose (an average of 65 months up to a max of 85 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants	35	35	28	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing Adverse Events (AEs) Leading to Withdrawal

End point title	Number of Participants Experiencing Adverse Events (AEs) Leading to Withdrawal ^[4]
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End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding),

symptom, or disease temporarily associated with the use of medicinal product, whether or not considered related to the investigational medicinal product.

End point type	Primary
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End point timeframe:

From first dose to 90-days post last dose (an average of 65 months up to a max of 85 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants	32	35	28	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing Adverse Events (AEs) of Special Interest

End point title	Number of Participants Experiencing Adverse Events (AEs) of Special Interest ^[5]
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End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of medicinal product, whether or not considered related to the investigational medicinal product.

End point type	Primary
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End point timeframe:

From first dose to 90-days post last dose (an average of 65 months up to a max of 85 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants				
Infections and infestations	19	26	19	
Neoplasms benign, malignant and unspecified	9	14	16	
Blood and lymphatic system disorders	0	0	1	
Nervous system disorders	0	2	1	

Eye disorders	5	2	2	
Cardiac disorders	0	1	2	
Hepatobiliary disorders	0	1	0	
Skin and subcutaneous tissue disorders	0	0	1	
Congenital, familial and genetic disorders	1	0	0	
Investigations	15	14	8	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Abnormalities in Blood Absolute Lymphocyte Count (ALC)

End point title	Number of Participants with Abnormalities in Blood Absolute Lymphocyte Count (ALC) ^[6]
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End point description:

An absolute lymphocyte count (ALC) is a part of a blood test that measures the number of lymphocytes, a type of white blood cell, in the blood. Lymphocytes help fight infections and diseases. Reductions in ALC levels for participants in this study is expected and is a primary pharmacodynamic effect of RPC1063.

LLN = Lower limit of normal

End point type	Primary
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End point timeframe:

From first dose up until last dose of study treatment (up to approximately 82 months)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	727	868	877	
Units: Participants				
ALC < 0.2 x 10 ⁹ /L	33	33	27	
ALC < 0.5 x 10 ⁹ /L	265	323	339	
ALC < 0.8 x 10 ⁹ /L	497	620	616	
ALC < LLN	592	703	704	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Abnormalities in White Blood Cell Count (WBC)

End point title	Number of Participants with Abnormalities in White Blood Cell Count (WBC) ^[7]
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End point description:

A white blood cell count is a part of a blood test that measures the number of white blood cells in the blood. White blood cells help fight infections and diseases.

LLN = Lower limit of normal

End point type	Primary
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End point timeframe:

From first dose up until last dose of study treatment (up to approximately 82 months)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	727	868	877	
Units: Participants				
Total WBC > 20 x 10 ⁹ /L	0	0	2	
Total WBC < 3 x 10 ⁹ /L	27	48	43	
Total WBC < 2 x 10 ⁹ /L	0	2	0	
Total WBC < 1 x 10 ⁹ /L	0	0	0	
Total WBC < LLN	92	107	108	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Abnormalities in Blood Absolute Neutrophil Count (ANC)

End point title	Number of Participants with Abnormalities in Blood Absolute Neutrophil Count (ANC) ^[8]
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End point description:

An absolute neutrophil count is a part of a blood test that measures the number of neutrophils, a type of white blood cell, in the blood. Neutrophils help fight infections and diseases.

End point type	Primary
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End point timeframe:

From first dose up until last dose of study treatment (up to approximately 82 months)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	727	868	877	
Units: Participants	0	2	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Abnormalities in Specific Liver Function Tests

End point title	Number of Participants with Abnormalities in Specific Liver Function Tests ^[9]
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End point description:

The number of participants with laboratory abnormalities in specific liver tests above ULN by category. ULN = Upper Limit of Normal.

End point type	Primary
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End point timeframe:

From first dose up until last dose of study treatment (up to approximately 82 months)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	728	875	880	
Units: Participants				
> 1 x ULN	311	353	353	
>= 2 x ULN	90	100	107	
>= 3 x ULN	32	30	29	
>= 4 x ULN	16	19	6	
>= 5 x ULN	8	12	0	
>= 10 x ULN	4	5	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Electrocardiogram (ECG) Result Outliers

End point title	Number of Participants with Electrocardiogram (ECG) Result Outliers ^[10]
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End point description:

An electrocardiogram (ECG) measures electrical activity of the heart to detect cardiac problems.

End point type	Primary
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End point timeframe:

From first dose to 28-days post last dose (an average of 63 months up to a max of 83 months)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	876	880	
Units: Participants				
QT > 480 (ms)	6	5	3	
QT > 500 (ms)	1	0	0	
QTcF > 450 (ms)	44	49	44	
QTcF > 480 (ms)	1	5	3	
QTcF > 500 (ms)	0	0	0	
QTcB > 450 (ms)	173	186	184	
QTcB > 480 (ms)	8	15	13	
QTcB > 500 (ms)	0	2	0	
Change from Baseline in QTcF >30 ms	134	140	120	
Change from Baseline in QTcF >60 ms	0	5	6	
Change from Baseline in QTcB >30 ms	183	215	205	
Change from Baseline in QTcB >60 ms	5	9	13	
Atrial Ventricular Block or Conduction Ratio, 2:1	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Clinically Relevant Abnormalities in Vital Signs

End point title	Number of Participants with Clinically Relevant Abnormalities in Vital Signs ^[11]
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End point description:

Vital signs included body temperature, sitting heart rate/pulse (HR), sitting systolic blood pressure (SBP), sitting diastolic blood pressure (DBP).

End point type	Primary
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End point timeframe:

At baseline and 60 months after first dose of study therapy

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	567	715	707	
Units: Participants				
Temp(C) >38.5 and incr frm BL >= 1	0	0	0	
HR(bpm) >120bpm post-BL or incr frm BL>20 bpm	15	19	26	
HR(bpm) >120 bpm post-BL if BL<=120 bpm	0	0	0	
HR(bpm) Incr from BL > 20 bpm	15	19	26	
HR(bpm) <45 bpm post-BL or decr from BL>20bpm	7	12	8	
HR(bpm) <45 bpm post-BL if BL >=45 bpm	0	0	0	
HR(bpm) Decr from BL >20 bpm	7	12	8	
SBP>180 mmHg post-BL or incr from BL>40 mmHg	3	5	5	
SBP >180 mmHg post-BL if BL<=180 mmHg	0	0	0	
SBP: Increase from BL>40 mmHg	3	5	5	
SBP<90 mmHg post-BL or decr from BL>30 mmHg	3	1	3	
SBP<90 mmHg post-BL if BL>=90 mmHg	1	0	0	
SBP: Decr from BL > 30 mmHg	2	1	3	
DBP>105 mmHg post-BL or incr from BL>30 mmHg	2	4	4	
DBP >105 mmHg post-BL if BL<=105 mmHg	1	2	3	
DBP: Increase from BBL>30 mmHg	1	2	2	
DBP<50 mmHg post-BL or decr from BL>30 mmHg	1	2	0	
DBP<50 mmHg post-BL if BL>=50 mmHg	0	0	0	
DBP: Decrease from BL>30 mmHg	1	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Physical Examination Abnormalities

End point title	Number of Participants with Physical Examination
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End point description:

The number of participants with abnormal physical examination results. The assessments included abdominal, extremity, head, heart, lungs, neck, neurological non-MS, other and skin assessments.

End point type	Primary
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End point timeframe:

At baseline and every 12 months thereafter up until 84 months post first dose.

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants				
Baseline - Abdominal	0	0	1	
Baseline - Extremities	3	2	8	
Baseline - Head	0	1	1	
Baseline - Heart	1	0	1	
Baseline - Lungs	0	1	2	
Baseline - Neck	0	1	3	
Baseline - Neurological-Non-MS	1	1	5	
Baseline - Other	2	6	4	
Baseline - Skin	17	17	16	
Month 12 - Abdominal	1	2	2	
Month 12 - Extremities	2	4	6	
Month 12 - Head	2	2	3	
Month 12 - Heart	3	0	0	
Month 12 - Lungs	0	0	1	
Month 12 - Neck	0	1	3	
Month 12 - Neurological-Non-MS	1	3	0	
Month 12 - Other	2	4	2	
Month 12 - Skin	25	24	21	
Month 24 - Abdominal	0	2	2	
Month 24 -Extremities	5	9	6	
Month 24 - Head	3	4	2	
Month 24 - Lungs	0	1	3	
Month 24 - Neck	1	1	2	
Month 24 - Neurological-Non-MS	2	1	3	
Month 24 - Other	2	3	3	
Month 24 - Skin	20	21	23	
Month 36 - Abdominal	1	1	1	
Month 36 - Extremities	5	5	7	
Month 36 - Head	1	0	4	
Month 36 - Heart	0	0	1	
Month 36 - Lungs	1	2	1	
Month 36 - Neck	1	1	0	
Month 36 - Neurological-Non-MS	1	1	4	
Month 36 - Other	4	4	4	
Month 36 - Skin	22	32	34	
Month 48 - Abdominal	0	0	1	
Month 48 - Extremities	4	7	5	
Month 48 - Head	1	2	1	
Month 48 - Heart	0	0	1	
Month 48 - Lungs	0	1	2	

Month 48 - Neck	0	1	0	
Month 48 - Neurological-Non-MS	3	1	0	
Month 48 - Other	2	3	4	
Month 48 - Skin	19	23	18	
Month 60 - Abdominal	1	2	0	
Month 60 - Extremities	4	9	11	
Month 60 - Head	1	1	1	
Month 60 - Heart	0	0	2	
Month 60 - Lungs	0	1	2	
Month 60 - Neck	2	0	0	
Month 60 - Neurological-Non-MS	2	1	4	
Month 60 - Other	3	4	1	
Month 60 - Skin	16	28	18	
Month 72 - Abdominal	1	2	2	
Month 72 - Extremities	4	5	5	
Month 72 - Head	0	1	1	
Month 72 - Heart	0	0	0	
Month 72 - Lungs	0	0	1	
Month 72 - Neck	1	0	0	
Month 72 - Neurological-Non-MS	2	2	2	
Month 72 - Other	5	3	2	
Month 72 - Skin	8	19	10	
Month 84 - Abdominal	0	1	0	
Month 84 - Extremities	0	1	1	
Month 84 - Skin	0	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Self-Identifying Suicidality by Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants Self-Identifying Suicidality by Columbia-Suicide Severity Rating Scale (C-SSRS) ^[13]
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End point description:

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a unique suicide risk assessment tool that supports suicide risk assessment through a series of simple, plain-language questions. The answers help users identify whether someone is at risk for suicide, assess the severity and immediacy of that risk, and gauge the level of support that the person needs.

End point type	Primary
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End point timeframe:

At baseline and every 3 months thereafter up until 78 months post first dose.

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	733	874	879	
Units: Participants				
At baseline (Suicidal Ideation or Behavior)	0	2	0	
At month 3 (Suicidal Ideation or Behavior)	2	1	1	
At month 6 (Suicidal Ideation or Behavior)	1	1	2	
At month 9 (Suicidal Ideation or Behavior)	3	0	1	
At month 12 (Suicidal Ideation or Behavior)	3	0	2	
At month 15 (Suicidal Ideation or Behavior)	0	0	1	
At month 18 (Suicidal Ideation or Behavior)	1	1	2	
At month 21 (Suicidal Ideation or Behavior)	1	0	1	
At month 24 (Suicidal Ideation or Behavior)	1	2	1	
At month 27 (Suicidal Ideation or Behavior)	0	0	0	
At month 33 (Suicidal Ideation or Behavior)	1	0	0	
At month 36 (Suicidal Ideation or Behavior)	2	1	0	
At month 39 (Suicidal Ideation or Behavior)	0	1	0	
At month 42 (Suicidal Ideation or Behavior)	0	0	1	
At month 45 (Suicidal Ideation or Behavior)	0	0	0	
At month 48 (Suicidal Ideation or Behavior)	2	0	1	
At month 54 (Suicidal Ideation or Behavior)	1	0	1	
At month 57 (Suicidal Ideation or Behavior)	0	0	0	
At month 60 (Suicidal Ideation or Behavior)	2	1	1	
At month 66 (Suicidal Ideation or Behavior)	1	2	1	
At month 69 (Suicidal Ideation or Behavior)	1	0	1	
At month 72 (Suicidal Ideation or Behavior)	1	0	1	
At month 78 (Suicidal Ideation or Behavior)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Change in Physician's Withdrawal Checklist (PWC-20) Score from Last Day on Treatment

End point title	Change in Physician's Withdrawal Checklist (PWC-20) Score from Last Day on Treatment ^[14]
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End point description:

End point type	Primary
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End point timeframe:

1, 4, 7, 14, 21, and 90 post last dose.

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Withdrawal Analysis Combination			
Subject group type	Subject analysis set			
Number of subjects analysed	95			
Units: PWS-20 Score				
arithmetic mean (standard deviation)				
End of Treatment	-0.1 (± 6.33)			
Follow-up Visit Day 1	-0.6 (± 5.06)			
Follow-up Visit Day 4	-0.5 (± 4.51)			
Follow-up Visit Day 7	-1.1 (± 4.33)			
Follow-up Visit Day 14	-0.4 (± 4.93)			
Follow-up Visit Day 21	-1.2 (± 5.31)			
Follow-up Visit Day 90	-0.7 (± 5.15)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in Hospital Anxiety and Depression Scale (HADS) Score from Last Day on Treatment

End point title	Change in Hospital Anxiety and Depression Scale (HADS) Score from Last Day on Treatment ^[15]
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End point description:

End point type	Primary
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End point timeframe:

1, 4, 7, 14, 21, and 90 days post last dose.

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Withdrawal Analysis Combination			
Subject group type	Subject analysis set			
Number of subjects analysed	96			
Units: HADS Score				
arithmetic mean (standard deviation)				
Depression - End of Treatment	0.3 (± 3.17)			
Depression - Follow-up Visit Day 1	-0.1 (± 2.15)			
Depression - Follow-up Visit Day 4	-0.1 (± 2.13)			
Depression - Follow-up Visit Day 7	-0.2 (± 2.29)			
Depression - Follow-up Visit Day 14	0.1 (± 2.36)			
Depression - Follow-up Visit Day 21	0.1 (± 2.35)			
Depression - 90-Day Safety Follow-up Visit	-0.2 (± 2.86)			
Anxiety - End of Treatment	-0.3 (± 2.76)			
Anxiety - Follow-up Visit Day 1	-0.5 (± 2.33)			
Anxiety - Follow-up Visit Day 4	-0.4 (± 2.30)			
Anxiety - Follow-up Visit Day 7	-0.8 (± 2.47)			
Anxiety - Follow-up Visit Day 14	-0.6 (± 2.17)			
Anxiety - Follow-up Visit Day 21	-0.7 (± 2.35)			
Anxiety -90-Day Safety Follow-up Visit	-0.7 (± 2.99)			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in Epworth Sleepiness Scale (ESS) Score from Last Day on Treatment

End point title	Changes in Epworth Sleepiness Scale (ESS) Score from Last Day on Treatment ^[16]
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End point description:

End point type	Primary
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End point timeframe:

1, 4, 7, 14, 21, and 90 days post last dose.

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Withdrawal Analysis Combination			
Subject group type	Subject analysis set			
Number of subjects analysed	96			
Units: ESS Score				
arithmetic mean (standard deviation)				
End of Treatment	0.4 (± 4.92)			
Follow-up Visit Day 1	-0.6 (± 4.28)			
Follow-up Visit Day 4	-0.5 (± 4.38)			
Follow-up Visit Day 7	-0.7 (± 4.25)			

Follow-up Visit Day 14	-0.9 (± 4.10)			
Follow-up Visit Day 21	-0.9 (± 4.42)			
Follow-up Visit Day 90	-0.8 (± 3.75)			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in Columbia-Suicide Severity Rating Scale (C-SSRS) Score from Last Day on Treatment

End point title	Changes in Columbia-Suicide Severity Rating Scale (C-SSRS) Score from Last Day on Treatment ^[17]
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End point description:

End point type	Primary
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End point timeframe:

1, 4, 7, 14, 21, and 90 days post last dose.

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Withdrawal Analysis Combination			
Subject group type	Subject analysis set			
Number of subjects analysed	250			
Units: Participants				
End of Treatment	3			
Follow-up Visit Day 1	0			
Follow-up Visit Day 4	0			
Follow-up Visit Day 7	0			
Follow-up Visit Day 14	0			
Follow-up Visit Day 21	0			
Safety Follow-up Visit (Day 28)	0			
Follow-up Visit Day 90	0			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in Vital Sign Values from Last Day on Treatment

End point title	Changes in Vital Sign Values from Last Day on Treatment ^[18]
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End point description:

End point type	Primary
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End point timeframe:

1, 4, 7, 14, 21, and 90 days post last dose.

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

End point values	Withdrawal Analysis Combination			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Unit Specific to Each Measure				
arithmetic mean (standard deviation)				
Systolic Blood Pressure: End of Treatment	-1.77 (± 11.189)			
Systolic Blood Pressure: Follow-up Visit Day 1	0.63 (± 8.311)			
Systolic Blood Pressure: Follow-up Visit Day 4	-0.04 (± 8.931)			
Systolic Blood Pressure: Follow-up Visit Day 7	0.82 (± 7.911)			
Systolic Blood Pressure: Follow-up Visit Day 14	-0.4 (± 8.128)			
Systolic Blood Pressure: Follow-up Visit Day 21	1.25 (± 9.029)			
Systolic Blood Pressure: Safety Follow-up	-0.72 (± 11.135)			
Systolic Blood Pressure: Follow-up Visit Day 90	-0.69 (± 10.865)			
Diastolic Blood Pressure: End of Treatment	-1.10 (± 8.356)			
Diastolic Blood Pressure: Follow-up Visit Day 1	-1.18 (± 8.218)			
Diastolic Blood Pressure: Follow-up Visit Day 4	-2.02 (± 7.760)			
Diastolic Blood Pressure: Follow-up Visit Day 7	-1.80 (± 7.275)			
Diastolic Blood Pressure: Follow-up Visit Day 14	-1.82 (± 7.643)			
Diastolic Blood Pressure: Follow-up Visit Day 21	-1.00 (± 8.181)			
Diastolic Blood Pressure Safety Follow-up	-1.21 (± 8.103)			
Diastolic Blood Pressure: Follow-up Day 90	-2.01 (± 7.689)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate (ARR)

End point title	Annualized Relapse Rate (ARR)
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End point description:

The Annualized Relapse Rate (ARR) is the average number of relapses per study arm in one year. A relapse is defined as the occurrence of new or worsening neurological symptoms attributable to multiple sclerosis (MS) and immediately preceded by a relatively stable or improving neurological state of at least 30 days. The adjusted ARR was based on the negative binomial regression model with parent treatment group, adjusted for region (Eastern Europe vs Rest of World), age at parent baseline, and the

parent baseline number of gadolinium-enhanced (GdE) lesions. The natural log transformation of time on treatment was used as an offset term to adjust for participants having different exposure times.

End point type	Secondary
End point timeframe:	
From first dose up until last dose of study treatment or data-cutoff date, whichever occurred first (up to approximately 87 months)	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Proportion of participants				
median (confidence interval 95%)	0.097 (0.078 to 0.121)	0.108 (0.088 to 0.133)	0.090 (0.073 to 0.111)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Relapse (TFR)

End point title	Time to First Relapse (TFR)
End point description:	
The time between first dose of study treatment and first relapse if experienced by a participant. A participant was censored if follow-up ended before a relapse occurred, whether due to the participant completing study, withdrawing from the study, or due to the cutoff of data collection for the analysis. The censor date was the date of the end of study or the date of the data cutoff for participant who were ongoing. Participants who withdraw from the study after the baseline visit were censored at the last known date while on study. Based on Kaplan-Meier product limit estimates. "99999" = N/A	
End point type	Secondary
End point timeframe:	
Overall: From first dose to end of study or data-cutoff date, whichever occurred first (up to approx 87 months); Specific Visits: At 2 weeks post first dose, then 3 months post first dose and every 3 months thereafter up until 81 months post first dose.	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	725	868	881	
Units: Days				
median (confidence interval 95%)				
Overall Study	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Week 2 (15 Days)	0.01 (0.01 to 0.03)	0.01 (0.01 to 0.02)	0.01 (0.00 to 0.01)
Month 3 (92 Days)	0.07 (0.05 to 0.09)	0.05 (0.03 to 0.06)	0.04 (0.03 to 0.05)
Month 6 (183 Days)	0.11 (0.09 to 0.13)	0.09 (0.07 to 0.11)	0.08 (0.06 to 0.10)
Month 9 (274 Days)	0.12 (0.10 to 0.15)	0.12 (0.10 to 0.14)	0.11 (0.09 to 0.13)
Month 12 (365 Days)	0.14 (0.12 to 0.17)	0.15 (0.12 to 0.17)	0.14 (0.11 to 0.16)
Month 15 (456 Days)	0.16 (0.13 to 0.19)	0.17 (0.14 to 0.19)	0.15 (0.13 to 0.17)
Month 18 (547 Days)	0.18 (0.15 to 0.21)	0.18 (0.16 to 0.21)	0.17 (0.15 to 0.20)
Month 21 (638 Days)	0.19 (0.16 to 0.22)	0.20 (0.17 to 0.23)	0.19 (0.16 to 0.21)
Month 24 (729 Days)	0.21 (0.18 to 0.24)	0.22 (0.19 to 0.25)	0.20 (0.18 to 0.23)
Month 27 (820 Days)	0.22 (0.19 to 0.25)	0.23 (0.20 to 0.26)	0.21 (0.19 to 0.24)
Month 30 (911 Days)	0.23 (0.20 to 0.27)	0.23 (0.21 to 0.26)	0.22 (0.20 to 0.25)
Month 33 (1002 Days)	0.24 (0.21 to 0.28)	0.25 (0.22 to 0.28)	0.23 (0.20 to 0.26)
Month 36 (1093 Days)	0.26 (0.23 to 0.29)	0.26 (0.23 to 0.29)	0.24 (0.21 to 0.27)
Month 39 (1184 Days)	0.27 (0.24 to 0.30)	0.26 (0.24 to 0.30)	0.25 (0.22 to 0.28)
Month 42 (1275 Days)	0.28 (0.25 to 0.32)	0.27 (0.24 to 0.30)	0.27 (0.24 to 0.30)
Month 45 (1366 Days)	0.29 (0.25 to 0.32)	0.28 (0.25 to 0.31)	0.28 (0.25 to 0.31)
Month 48 (1457 Days)	0.29 (0.26 to 0.32)	0.29 (0.26 to 0.32)	0.29 (0.26 to 0.32)
Month 51 (1548 Days)	0.30 (0.26 to 0.33)	0.29 (0.26 to 0.32)	0.29 (0.26 to 0.32)
Month 54 (1639 Days)	0.30 (0.27 to 0.34)	0.30 (0.27 to 0.33)	0.30 (0.27 to 0.34)
Month 57 (1730 Days)	0.30 (0.27 to 0.34)	0.30 (0.27 to 0.34)	0.31 (0.28 to 0.34)
Month 60 (1821 Days)	0.31 (0.28 to 0.35)	0.31 (0.28 to 0.34)	0.32 (0.29 to 0.35)
Month 63 (1912 Days)	0.32 (0.28 to 0.35)	0.31 (0.28 to 0.35)	0.33 (0.30 to 0.36)
Month 66 (2003 Days)	0.32 (0.29 to 0.36)	0.32 (0.29 to 0.36)	0.33 (0.30 to 0.36)
Month 69 (2094 Days)	0.33 (0.29 to 0.36)	0.33 (0.30 to 0.36)	0.33 (0.30 to 0.37)
Month 72 (2185 Days)	0.33 (0.29 to 0.36)	0.33 (0.30 to 0.37)	0.33 (0.30 to 0.37)
Month 75 (2276 Days)	0.33 (0.29 to 0.36)	0.33 (0.30 to 0.37)	0.34 (0.30 to 0.37)
Month 78 (2367 Days)	0.33 (0.29 to 0.36)	0.33 (0.30 to 0.37)	0.34 (0.30 to 0.37)
Month 81 (2458 Days)	0 (0 to 0)	0.33 (0.30 to 0.37)	0.34 (0.30 to 0.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Onset of Disability Progression as Defined by a Sustained Worsening in Expanded Disability Status Scale (EDSS)

End point title	Time to Onset of Disability Progression as Defined by a Sustained Worsening in Expanded Disability Status Scale (EDSS)
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End point description:

Multiple sclerosis (MS) disability progression is defined as a sustained worsening in EDSS of 1.0 points or more from baseline, confirmed after a 3-month and 6-month period. The EDSS is a standardized method, widely accepted, numerical scale used to evaluate disability in people with multiple sclerosis (MS). The EDSS is evaluated according to signs and symptoms observed during a standard neurological examination. These clinical observations are classified in 7 FS scales, each of them grading signs and symptoms for different neurological functions: pyramidal, cerebellar, brainstem, sensory, bowel or bladder, visual, and cerebral.

Derived using Kaplan-Meier estimates. "99999" = N/A

End point type	Secondary
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End point timeframe:

At 3 and 6 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	160	146	
Units: Days				
median (confidence interval 95%)				
Month 3	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Month 6	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Free of Gadolinium-Enhanced (GdE) Brain Lesions at Each Visit

End point title	Number of Participants Free of Gadolinium-Enhanced (GdE) Brain Lesions at Each Visit
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End point description:

Number of participants without gadolinium enhanced (GdE) brain MRI lesions at each visit. Increased numbers of GdE lesions indicates an increase in the in the amount of active inflammation at the site and may be indicative of progressive disease.

Based on cumulative number of GdE lesions at a participant level.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug ITT Population	Parent Treatment Group: RPC1063 0.5 mg ITT	Parent Treatment Group: RPC1063 1.0 mg ITT	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	740	756	760	
Units: Participants				
Baseline	609	662	538	
Month 12	644	627	622	
Month 24	601	596	582	
Month 36	576	569	538	
Month 48	518	517	569	
Month 60	528	512	478	
Month 72	145	149	121	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Free of New or Enlarging T2 Lesions at Each Visit

End point title	Number of Participants Free of New or Enlarging T2 Lesions at Each Visit
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End point description:

Number of participants without new or enlarging T2 brain MRI lesions at each visit. Some multiple Sclerosis (MS) lesions appear as bright spots in a T2-weighted MRI scan - these are called T2 lesions. The presence of new or larger T2 lesions may mean the participant is at higher risk of disability and may have a less favorable long-term outcome.

Based on cumulative number of new or enlarging T2 lesions at a participant level.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	696	722	726	
Units: Participants				
Month 12	322	400	419	
Month 24	260	323	338	
Month 36	220	264	271	
Month 48	204	223	223	
Month 60	177	213	209	

Month 72	53	59	57	
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Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Normalized Brain Volume (Atrophy) on Brain MRI Scans from Baseline at Each Visit

End point title	Percent Change in Normalized Brain Volume (Atrophy) on Brain MRI Scans from Baseline at Each Visit
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End point description:

Percent change in normalized brain volume (Atrophy) on brain MRI scans from baseline at each visit. Brain atrophy can be seen in the earliest stages of multiple sclerosis (MS) and is a reliable predictor of future physical and cognitive disability.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until approximately 87 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	596	611	623	
Units: Percent Volume Change from Baseline				
arithmetic mean (standard deviation)				
Month 12	-0.407 (± 0.731)	-0.359 (± 0.607)	-0.385 (± 0.602)	
Month 24	-0.702 (± 0.809)	-0.657 (± 0.713)	-0.671 (± 0.706)	
Month 36	-0.992 (± 0.882)	-0.947 (± 0.825)	-0.977 (± 0.764)	
Month 48	-1.241 (± 1.012)	-1.214 (± 0.980)	-1.233 (± 0.949)	
Month 60	-1.485 (± 1.079)	-1.478 (± 1.014)	-1.544 (± 1.017)	
Month 72	-1.889 (± 1.288)	-1.696 (± 1.118)	-1.922 (± 1.290)	
End of Treatment	-1.283 (± 1.206)	-1.298 (± 1.133)	-1.355 (± 1.121)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Multiple Sclerosis Functional Composite (MSFC) Score from Baseline at Each Applicable Visit

End point title	Change in Multiple Sclerosis Functional Composite (MSFC) Score from Baseline at Each Applicable Visit
End point description:	
The MSFC is a three-part tool used in clinical studies to measure disability progression in patients with multiple sclerosis (MS). It includes the assessment of leg function, arm and hand function, and cognitive function. Scores from each of the three components are converted into Z-scores and averaged to create an overall composite score. "99999" = N/A	
End point type	Secondary
End point timeframe:	
At baseline and every 12 months thereafter up until 84 months post first dose.	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	702	721	732	
Units: MSFC Z-Score Change from Baseline				
arithmetic mean (standard deviation)				
MSFC Z Score Month 12	0.058 (± 2.540)	-0.085 (± 0.488)	-0.064 (± 0.618)	
MSFC Z Score Month 24	-0.072 (± 0.855)	-0.082 (± 0.615)	-0.086 (± 0.632)	
MSFC Z Score Month 36	-0.105 (± 0.876)	-0.100 (± 0.529)	-0.109 (± 0.656)	
MSFC Z Score Month 48	-0.162 (± 1.025)	-0.148 (± 0.611)	-0.103 (± 1.460)	
MSFC Z Score Month 60	-0.182 (± 1.062)	-0.174 (± 0.675)	-0.148 (± 0.580)	
MSFC Z Score Month 72	-0.248 (± 1.256)	-0.239 (± 0.745)	-0.219 (± 0.672)	
MSFC Z Score Month 84	0 (± 0)	-0.099 (± 99999)	0 (± 0)	
MSFC Z Score (LCLA) Month 12	0.043 (± 1.919)	-0.059 (± 0.402)	-0.055 (± 0.483)	
MSFC Z Score (LCLA) Month 24	-0.056 (± 0.655)	-0.064 (± 0.483)	-0.074 (± 0.509)	
MSFC Z Score (LCLA) Month 36	-0.097 (± 0.686)	-0.089 (± 0.447)	-0.103 (± 0.542)	
MSFC Z Score (LCLA) Month 48	-0.158 (± 0.796)	-0.149 (± 0.525)	-0.103 (± 1.125)	
MSFC Z Score (LCLA) Month 60	-0.175 (± 0.837)	-0.181 (± 0.572)	-0.153 (± 0.505)	
MSFC Z Score (LCLA) Month 72	-0.237 (± 0.983)	-0.250 (± 0.624)	-0.213 (± 0.590)	
MSFC Z Score (LCLA) Month 84	0 (± 0)	-0.103 (± 99999)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Multiple Sclerosis Quality of Life 54 Score from Baseline at Each Applicable Visit

End point title	Change in Multiple Sclerosis Quality of Life 54 Score from Baseline at Each Applicable Visit
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End point description:

Multiple Sclerosis Quality of Life 54 (MSQOL-54) is a widely-used, health-related quality of life (HRQOL) instrument specific for multiple sclerosis (MS). This 54-item instrument generates 12 subscales along with two summary scores, and two additional single-item measures. The subscales are: physical function, role limitations-physical, role limitations-emotional, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, overall quality of life, and sexual function. "99999" = N/A

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 84 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	659	678	678	
Units: MSQOL-54 Score Change from Baseline				
arithmetic mean (standard deviation)				
Month 12	0.1 (± 10.68)	-0.1 (± 10.55)	0.2 (± 9.85)	
Month 24	0.8 (± 11.51)	-0.6 (± 10.76)	-0.3 (± 11.25)	
Month 36	0.1 (± 12.20)	-0.6 (± 11.23)	-0.4 (± 12.37)	
Month 48	-0.3 (± 12.60)	-1.4 (± 12.66)	-1.4 (± 12.71)	
Month 60	-1.1 (± 13.27)	-2.7 (± 13.11)	-2.1 (± 12.62)	
Month 72	-1.6 (± 14.97)	-3.0 (± 13.42)	-3.0 (± 13.88)	
Month 84	0 (± 0)	-0.3 (± 99999)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Volume of Gadolinium Enhanced T1 Lesions

End point title	Change from Baseline in Volume of Gadolinium Enhanced T1 Lesions
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End point description:

Change from baseline in volume of gadolinium enhanced T1 lesions. T1-lesions are permanently damaged areas of the brain that appear as dark spots or "black holes" on a type of MRI scan. The growth of T1 lesions may mean the participant's Multiple Sclerosis (MS) is progressing.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	695	723	725	
Units: Volume (cm ³) Change from Baseline				
arithmetic mean (standard deviation)				
Month 12	-0.092 (± 0.435)	-0.015 (± 0.229)	-0.004 (± 0.180)	
Month 24	-0.099 (± 0.431)	-0.017 (± 0.193)	0.009 (± 0.264)	
Month 36	-0.089 (± 0.485)	-0.018 (± 0.183)	0.012 (± 0.237)	
Month 48	-0.081 (± 0.467)	-0.012 (± 0.204)	0.017 (± 0.252)	
Month 60	-0.090 (± 0.448)	-0.017 (± 0.217)	0.000 (± 0.189)	
Month 72	-0.044 (± 0.145)	0.003 (± 0.157)	0.014 (± 0.307)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Volume of T2 Lesions

End point title	Change from Baseline in Volume of T2 Lesions
End point description:	
Some multiple Sclerosis (MS) lesions appear as bright spots in a T2-weighted MRI scan - these are called T2 lesions. Larger T2 lesions may mean the participant is at higher risk of disability and may have a less favorable long-term outcome.	
End point type	Secondary
End point timeframe:	
At baseline and every 12 months thereafter up until 72 months post first dose.	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	696	723	726	
Units: Volume (cm ³) Change from Baseline				
arithmetic mean (standard deviation)				

Month 12	0.190 (± 1.498)	0.174 (± 1.154)	0.278 (± 1.384)	
Month 24	0.307 (± 1.633)	0.303 (± 1.503)	0.518 (± 2.294)	
Month 36	0.536 (± 2.218)	0.456 (± 1.597)	0.711 (± 2.540)	
Month 48	0.695 (± 2.805)	0.583 (± 1.975)	0.952 (± 2.945)	
Month 60	0.709 (± 2.907)	0.683 (± 2.470)	0.987 (± 3.197)	
Month 72	0.889 (± 2.760)	0.557 (± 2.465)	1.234 (± 4.307)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Volume of Unenhancing T1 Lesions

End point title	Change from Baseline in Volume of Unenhancing T1 Lesions
End point description:	
Change from baseline in volume of unenhancing T1 lesions. T1-lesions are permanently damaged areas of the brain that appear as dark spots or "black holes" on a type of MRI scan. The growth of T1 lesions may mean the participant's Multiple Sclerosis (MS) is progressing.	
End point type	Secondary
End point timeframe:	
At baseline and every 12 months thereafter up until 72 months post first dose.	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	695	723	726	
Units: Volume (cm ³) Change from Baseline				
arithmetic mean (standard deviation)				
Month 12	-0.625 (± 2.012)	-0.772 (± 1.792)	-0.760 (± 1.869)	
Month 24	-0.192 (± 1.837)	-0.465 (± 1.735)	-0.455 (± 1.758)	
Month 36	-0.482 (± 2.913)	-0.618 (± 2.430)	-0.583 (± 2.249)	
Month 48	-0.398 (± 3.025)	-0.423 (± 2.439)	-0.403 (± 2.171)	
Month 60	-0.261 (± 2.885)	-0.356 (± 2.679)	-0.209 (± 2.134)	
Month 72	-0.047 (± 2.209)	-0.372 (± 3.257)	-0.256 (± 2.036)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of New Unenhancing T1 Lesions

End point title	Number of New Unenhancing T1 Lesions
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End point description:

Number of new unenhancing T1 lesions. T1-lesions are permanently damaged areas of the brain that appear as dark spots or "black holes" on a type of MRI scan. The appearance of new T1 lesions may mean the participant's MS is progressing.

Derived as the cumulative number of new or enlarging T1 lesions relative to baseline at a participant level.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	695	722	725	
Units: New or Enlarging Lesions.				
arithmetic mean (standard deviation)				
Month 12	1.9 (± 4.66)	1.1 (± 2.86)	1.2 (± 3.16)	
Month 24	2.7 (± 6.30)	1.8 (± 5.04)	2.2 (± 5.24)	
Month 36	3.6 (± 8.41)	2.5 (± 7.04)	3.0 (± 7.55)	
Month 48	4.6 (± 11.02)	3.3 (± 8.67)	4.3 (± 10.56)	
Month 60	4.8 (± 11.43)	3.9 (± 10.18)	4.9 (± 12.39)	
Month 72	4.5 (± 10.11)	3.2 (± 8.76)	5.8 (± 16.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Number of New or Enlarging Hyperintense T2-Weighted Brain MRI Lesions Per Scan at Each Visit

End point title	Average Number of New or Enlarging Hyperintense T2-Weighted Brain MRI Lesions Per Scan at Each Visit
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End point description:

Adjusted Mean of new enlarging T2 lesions per scan at each visit. Based on a negative binomial regression model, adjusted for parent study, region (Eastern Europe vs. Rest of the World), age at Baseline, and baseline number of GdE lesions. The natural log transformation of the number of available MRI scans per visit is used as an offset term.

T2 Magnetic Resonance Imaging (MRI) sequences are used to highlight areas of demyelination in brain neurons, which happens when the outer layer of the neurons is damaged due to multiple sclerosis (MS) activity. T2 sequences can be used to count the total number of MS lesions, which look like bright white spots on T2 sequences, and can be called "hyperintense".

End point type	Secondary
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End point timeframe:

At 12 months post first dose and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug ITT Population	Parent Treatment Group: RPC1063 0.5 mg ITT	Parent Treatment Group: RPC1063 1.0 mg ITT	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	696	722	726	
Units: New or Enlarging Lesions per Scan				
arithmetic mean (confidence interval 95%)				
Month 12	1.532 (1.309 to 1.792)	1.163 (0.995 to 1.360)	1.302 (1.116 to 1.519)	
Month 24	1.254 (1.072 to 1.466)	1.005 (0.862 to 1.172)	1.190 (1.022 to 1.385)	
Month 36	1.136 (0.963 to 1.340)	1.021 (0.872 to 1.197)	1.142 (0.976 to 1.335)	
Month 48	0.935 (0.786 to 1.112)	0.915 (0.770 to 1.087)	1.044 (0.883 to 1.234)	
Month 60	0.791 (0.661 to 0.948)	0.864 (0.728 to 1.025)	0.935 (0.787 to 1.110)	
Month 72	0.800 (0.566 to 1.132)	0.780 (0.567 to 1.074)	0.926 (0.684 to 1.255)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average Number of Gadolinium-Enhanced (GdE) Brain MRI Lesions Per Scan at Each Visit

End point title	Average Number of Gadolinium-Enhanced (GdE) Brain MRI Lesions Per Scan at Each Visit
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End point description:

Number of gadolinium-enhanced (GdE) (also called GdE enhanced T1) brain MRI lesions per scan at each visit.

Increased numbers of GdE lesions indicates an increase in the in the amount of active inflammation at the site and may be indicative of progressive disease.

Based on a negative binomial regression model, adjusted for parent study, region (Eastern Europe vs. Rest of the World), age at Baseline, and Baseline number of GdE lesions.

End point type	Secondary
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End point timeframe:

At baseline and every 12 months thereafter up until 72 months post first dose.

End point values	Parent Treatment Group IFN-B-1a 30 ug ITT Population	Parent Treatment Group: RPC1063 0.5 mg ITT	Parent Treatment Group: RPC1063 1.0 mg ITT	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	740	756	760	
Units: New or Enlarging Lesions				
arithmetic mean (confidence interval 95%)				
Baseline	0.460 (0.369 to 0.573)	0.244 (0.193 to 0.308)	0.177 (0.138 to 0.226)	
Month 12	0.106 (0.076 to 0.147)	0.130 (0.097 to 0.175)	0.205 (0.155 to 0.273)	
Month 24	0.138 (0.099 to 0.192)	0.149 (0.109 to 0.205)	0.224 (0.166 to 0.302)	
Month 36	0.194 (0.134 to 0.281)	0.155 (0.109 to 0.221)	0.243 (0.173 to 0.342)	
Month 48	0.230 (0.163 to 0.325)	0.161 (0.108 to 0.241)	0.245 (0.170 to 0.355)	
Month 60	0.074 (0.043 to 0.125)	0.062 (0.037 to 0.104)	0.076 (0.046 to 0.126)	
Month 72	0.099 (0.044 to 0.224)	0.102 (0.049 to 0.213)	0.082 (0.038 to 0.177)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants Who Were Relapse Free

End point title	Number of Participants Who Were Relapse Free
End point description: The number of participants who did not experience relapse. A relapse is defined as the occurrence of new or worsening neurological symptoms attributable to multiple sclerosis (MS) and immediately preceded by a relatively stable or improving neurological state of at least 30 days.	
End point type	Other pre-specified
End point timeframe: From first dose to last dose of study treatment or data-cutoff date, whichever occurred first (up to approximately 87 months)	

End point values	Parent Treatment Group IFN-B-1a 30 ug	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: RPC1063 1.0 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	877	881	
Units: Participants	513	605	605	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All events from first dose of OLE up to and including last dose +90 days

Adverse event reporting additional description:

Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Parent Treatment Group: Placebo-RPC1063 0.5 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063 to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: Placebo-RPC1063 1 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063 to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: RPC1063 1 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: RPC1063 0.5 mg
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Reporting group title	Parent Treatment Group: IFN beta-1a 30 ug
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Reporting group description:

Participants received a 7-day titration regimen of RPC1063, as applicable to reach the targeted dose of 1.0 mg which was taken by mouth once per day until the end of the trial or until the Sponsor discontinued the development program. Participants were instructed to take RPC1063 at approximately the same time each day with or without food.

Serious adverse events	Parent Treatment Group: Placebo-RPC1063 0.5 mg	Parent Treatment Group: Placebo-RPC1063 1 mg	Parent Treatment Group: RPC1063 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 37 (18.92%)	3 / 35 (8.57%)	131 / 846 (15.48%)
number of deaths (all causes)	0	0	5
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiomyxoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Bladder cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bladder papilloma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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

Breast cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Borderline serous tumour of ovary			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Leiomyoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Malignant melanoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatofibrosarcoma protuberans			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stromal tumour			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Invasive breast carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	3 / 846 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ovarian germ cell teratoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurilemmoma benign			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Malignant neoplasm progression			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Neoplasm malignant			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Myxoid liposarcoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanocytic naevus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Nephroblastoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	0 / 846 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the cervix			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Seminoma			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Thrombophlebitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Surgical and medical procedures			
Medical device removal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pregnancy, puerperium and perinatal			

conditions			
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Abortion missed			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Abortion spontaneous			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Anembryonic gestation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Sudden death			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Swelling face			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Social circumstances			
Miscarriage of partner			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Abnormal uterine bleeding			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Menometrorrhagia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Hydrosalpinx			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Heavy menstrual bleeding			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cervical dysplasia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast dysplasia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Adnexa uteri cyst			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenomyosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive tract disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Rectocele			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Prostatitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Polycystic ovaries			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Perineal fistula			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Varicocele			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
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, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Epistaxis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pulmonary embolism			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pulmonary sarcoidosis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pleurisy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Cardiovascular somatic symptom disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Adjustment disorder with mixed anxiety and depressed mood			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute stress disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Depression			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Suicide attempt			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Product issues			
Needle issue			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Chronic hepatitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary polyp			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cholecystitis acute			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	3 / 846 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
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			
Concussion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Craniocerebral injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Eye injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Femur fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Forearm fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Fracture displacement			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Hand fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Intentional overdose			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Joint injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ligament sprain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Road traffic accident			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Rib fracture			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
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 contusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pneumothorax traumatic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nerve injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Upper limb fracture			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Tibia fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Thermal burn			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Tendon rupture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Spinal fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Sebaceous naevus			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Kidney duplex			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Hydrocele			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cryptorchism			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Bradycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Adams-Stokes syndrome			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Sinoatrial block			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cerebral haematoma			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cerebellar infarction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Altered state of consciousness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Cervical radiculopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Migraine			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	3 / 846 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (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
Ischaemic stroke			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsia partialis continua			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Encephalitis autoimmune			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (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
Headache			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Radicular pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Peroneal nerve palsy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Paraparesis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Optic neuritis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Noninfective encephalitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Neurological decompensation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Multiple sclerosis relapse			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Restless legs syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Sensory disturbance			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Seizure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Immune thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microcytic anaemia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Deafness neurosensory			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Otosclerosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Choroiditis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Iridocyclitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blepharal pigmentation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal polyp			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Duodenal perforation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Colitis ulcerative			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	0 / 846 (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
Abdominal pain			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Abdominal hernia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 inflammation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Enteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Gastric ulcer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric disorder			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Gastritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Inflammatory bowel disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Large intestine polyp			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (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
Pancreatitis acute			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ranula			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Tooth loss			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Decubitus ulcer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Psoriasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Urticaria			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
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			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Calculus urinary			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Haematuria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney hypermobility			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Urogenital fistula			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ureteric stenosis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
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 colic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Ureterolithiasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Hyperadrenocorticism			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Goitre			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Musculoskeletal and connective tissue disorders			
Bursal fluid accumulation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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

Back pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Connective tissue disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Intervertebral disc disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondromalacia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Neck pain			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Mandibular mass			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Spondylolisthesis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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			
Abdominal wall infection			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
COVID-19			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	7 / 846 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Chronic hepatitis B			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Chronic sinusitis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	10 / 846 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 staphylococcal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Epididymitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	2 / 846 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Echinococcosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Diverticulitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Dacryocystitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Otitis media acute			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Orchitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	0 / 846 (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
Lyme disease			

subjects affected / exposed	0 / 37 (0.00%)	1 / 35 (2.86%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Injection site abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Hepatitis A			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
HIV infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Measles			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingo-oophoritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Salpingitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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 tract infection viral			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pyelonephritis chronic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pneumonia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	7 / 846 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Sepsis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic shock syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Tonsillitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Staphylococcal infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Septic shock			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	1 / 846 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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
Malnutrition			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	0 / 846 (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	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: IFN beta-1a 30 ug	
Total subjects affected by serious adverse events			
subjects affected / exposed	132 / 840 (15.71%)	108 / 736 (14.67%)	
number of deaths (all causes)	5	6	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiomyxoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder papilloma			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 840 (0.12%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Borderline serous tumour of ovary			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatofibrosarcoma protuberans			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian germ cell teratoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurilemmoma benign			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myxoid liposarcoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanocytic naevus			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephroblastoma			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	5 / 840 (0.60%)	6 / 736 (0.82%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the cervix			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seminoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Medical device removal			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	1 / 840 (0.12%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anembryonic gestation			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Swelling face			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Miscarriage of partner			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menometrorrhagia			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrosalpinx			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heavy menstrual bleeding			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix disorder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast dysplasia			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adnexa uteri cyst			
subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive tract disorder			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycystic ovaries			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal fistula			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicocele			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Cardiovascular somatic symptom disorder			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder with mixed anxiety and depressed mood			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute stress disorder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	4 / 840 (0.48%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Needle issue			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Chronic hepatitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary polyp			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ankle fracture			
subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Eye injury			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (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 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body in gastrointestinal tract			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			

subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve injury			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 840 (0.00%)	3 / 736 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
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 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Sebaceous naevus			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney duplex			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptorchism			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adams-Stokes syndrome			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinoatrial block			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
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	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haematoma			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	3 / 840 (0.36%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsia partialis continua			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis autoimmune			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular pain			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Noninfective encephalitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological decompensation			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis relapse			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless legs syndrome			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory disturbance			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 840 (0.24%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otosclerosis			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Choroiditis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iridocyclitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blepharal pigmentation			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal polyp			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids thrombosed			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric disorder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	2 / 840 (0.24%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ranula			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth loss			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney hypermobility			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic bladder			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urogenital fistula			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperadrenocorticism			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (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			
Bursal fluid accumulation			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	4 / 840 (0.48%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Connective tissue disorder			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Foot deformity			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 840 (0.00%)	3 / 736 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondromalacia			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 840 (0.36%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mandibular mass			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			

subjects affected / exposed	1 / 840 (0.12%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall infection			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	8 / 840 (0.95%)	4 / 736 (0.54%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Abscess limb			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatitis B			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	4 / 840 (0.48%)	3 / 736 (0.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	6 / 840 (0.71%)	4 / 736 (0.54%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis staphylococcal			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 840 (0.12%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Echinococcosis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryocystitis			

subjects affected / exposed	2 / 840 (0.24%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lyme disease			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injection site abscess			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV infection			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Measles			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingo-oophoritis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 840 (0.24%)	3 / 736 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 840 (0.12%)	4 / 736 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 840 (0.00%)	2 / 736 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic shock syndrome			

subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 840 (0.00%)	0 / 736 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 840 (0.00%)	1 / 736 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 840 (0.12%)	0 / 736 (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	Parent Treatment Group: Placebo-RPC1063 0.5 mg	Parent Treatment Group: Placebo-RPC1063 1 mg	Parent Treatment Group: RPC1063 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 37 (72.97%)	26 / 35 (74.29%)	659 / 846 (77.90%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 37 (5.41%)	2 / 35 (5.71%)	6 / 846 (0.71%)
occurrences (all)	2	2	6
Melanocytic naevus			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	12 / 846 (1.42%)
occurrences (all)	2	1	13
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 37 (13.51%)	2 / 35 (5.71%)	60 / 846 (7.09%)
occurrences (all)	5	2	67
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 37 (5.41%)	3 / 35 (8.57%)	29 / 846 (3.43%)
occurrences (all)	2	3	30
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	6 / 846 (0.71%)
occurrences (all)	0	2	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	30 / 846 (3.55%)
occurrences (all)	2	0	34
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 37 (0.00%)	4 / 35 (11.43%)	29 / 846 (3.43%)
occurrences (all)	0	4	34
Depression			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	41 / 846 (4.85%)
occurrences (all)	0	2	45

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 37 (8.11%)	3 / 35 (8.57%)	34 / 846 (4.02%)
occurrences (all)	3	3	44
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	15 / 846 (1.77%)
occurrences (all)	2	1	15
Blood cholesterol increased			
subjects affected / exposed	0 / 37 (0.00%)	4 / 35 (11.43%)	8 / 846 (0.95%)
occurrences (all)	0	4	8
Blood triglycerides increased			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	3 / 846 (0.35%)
occurrences (all)	0	2	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	4 / 35 (11.43%)	61 / 846 (7.21%)
occurrences (all)	1	4	85
Low density lipoprotein increased			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	4 / 846 (0.47%)
occurrences (all)	0	3	4
Lymphocyte count decreased			
subjects affected / exposed	7 / 37 (18.92%)	2 / 35 (5.71%)	81 / 846 (9.57%)
occurrences (all)	8	2	104
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	13 / 846 (1.54%)
occurrences (all)	0	3	20
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	3 / 846 (0.35%)
occurrences (all)	0	2	3
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	20 / 846 (2.36%)
occurrences (all)	1	2	21
Muscle spasticity			

subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	13 / 846 (1.54%)
occurrences (all)	0	2	14
Headache			
subjects affected / exposed	2 / 37 (5.41%)	7 / 35 (20.00%)	144 / 846 (17.02%)
occurrences (all)	2	25	298
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 37 (10.81%)	4 / 35 (11.43%)	36 / 846 (4.26%)
occurrences (all)	7	4	37
Lymphopenia			
subjects affected / exposed	3 / 37 (8.11%)	6 / 35 (17.14%)	73 / 846 (8.63%)
occurrences (all)	6	8	99
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	12 / 846 (1.42%)
occurrences (all)	0	2	13
Gastritis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	11 / 846 (1.30%)
occurrences (all)	1	2	12
Diarrhoea			
subjects affected / exposed	1 / 37 (2.70%)	4 / 35 (11.43%)	25 / 846 (2.96%)
occurrences (all)	1	5	31
Haemorrhoids			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	7 / 846 (0.83%)
occurrences (all)	2	0	7
Vomiting			
subjects affected / exposed	1 / 37 (2.70%)	3 / 35 (8.57%)	7 / 846 (0.83%)
occurrences (all)	1	3	16
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 37 (2.70%)	2 / 35 (5.71%)	4 / 846 (0.47%)
occurrences (all)	1	2	4
Dermatitis allergic			
subjects affected / exposed	2 / 37 (5.41%)	0 / 35 (0.00%)	5 / 846 (0.59%)
occurrences (all)	2	0	5
Renal and urinary disorders			

Urinary incontinence subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 35 (2.86%) 1	5 / 846 (0.59%) 5
Nephrolithiasis subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 35 (0.00%) 0	3 / 846 (0.35%) 3
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 3	3 / 35 (8.57%) 4	32 / 846 (3.78%) 41
Back pain subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 7	6 / 35 (17.14%) 8	71 / 846 (8.39%) 103
Arthralgia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 2	3 / 35 (8.57%) 4	61 / 846 (7.21%) 67
Infections and infestations			
Herpes zoster subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	2 / 35 (5.71%) 2	12 / 846 (1.42%) 12
COVID-19 subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 8	7 / 35 (20.00%) 7	136 / 846 (16.08%) 148
Bronchitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	3 / 35 (8.57%) 3	55 / 846 (6.50%) 68
Viral infection subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 35 (5.71%) 2	3 / 846 (0.35%) 3
Urinary tract infection subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 11	3 / 35 (8.57%) 6	58 / 846 (6.86%) 97
Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 7	8 / 35 (22.86%) 11	97 / 846 (11.47%) 143
Sinusitis			

subjects affected / exposed	1 / 37 (2.70%)	0 / 35 (0.00%)	30 / 846 (3.55%)
occurrences (all)	1	0	38
Respiratory tract infection viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 35 (0.00%)	46 / 846 (5.44%)
occurrences (all)	0	0	69
Respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	1 / 35 (2.86%)	53 / 846 (6.26%)
occurrences (all)	2	1	82
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	3 / 35 (8.57%)	35 / 846 (4.14%)
occurrences (all)	0	3	47
Nasopharyngitis			
subjects affected / exposed	5 / 37 (13.51%)	9 / 35 (25.71%)	177 / 846 (20.92%)
occurrences (all)	7	20	295
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	4 / 35 (11.43%)	24 / 846 (2.84%)
occurrences (all)	0	7	33
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 35 (5.71%)	11 / 846 (1.30%)
occurrences (all)	0	2	11
Hypercholesterolaemia			
subjects affected / exposed	1 / 37 (2.70%)	3 / 35 (8.57%)	33 / 846 (3.90%)
occurrences (all)	1	4	36

Non-serious adverse events	Parent Treatment Group: RPC1063 0.5 mg	Parent Treatment Group: IFN beta-1a 30 ug	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	663 / 840 (78.93%)	598 / 736 (81.25%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	8 / 840 (0.95%)	11 / 736 (1.49%)	
occurrences (all)	8	11	
Melanocytic naevus			
subjects affected / exposed	8 / 840 (0.95%)	6 / 736 (0.82%)	
occurrences (all)	8	6	
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	81 / 840 (9.64%) 93	76 / 736 (10.33%) 82	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	27 / 840 (3.21%) 30	17 / 736 (2.31%) 17	
Immune system disorders Immunisation reaction subjects affected / exposed occurrences (all)	9 / 840 (1.07%) 12	5 / 736 (0.68%) 5	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	32 / 840 (3.81%) 34	18 / 736 (2.45%) 21	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	26 / 840 (3.10%) 28 45 / 840 (5.36%) 54	28 / 736 (3.80%) 30 38 / 736 (5.16%) 43	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood cholesterol increased subjects affected / exposed occurrences (all) Blood triglycerides increased subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased	40 / 840 (4.76%) 54 20 / 840 (2.38%) 24 7 / 840 (0.83%) 7 3 / 840 (0.36%) 3 Gamma-glutamyltransferase increased	46 / 736 (6.25%) 67 23 / 736 (3.13%) 32 5 / 736 (0.68%) 5 4 / 736 (0.54%) 4 Gamma-glutamyltransferase increased	

subjects affected / exposed	63 / 840 (7.50%)	71 / 736 (9.65%)	
occurrences (all)	82	94	
Low density lipoprotein increased			
subjects affected / exposed	3 / 840 (0.36%)	1 / 736 (0.14%)	
occurrences (all)	3	1	
Lymphocyte count decreased			
subjects affected / exposed	77 / 840 (9.17%)	68 / 736 (9.24%)	
occurrences (all)	106	86	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 840 (0.95%)	11 / 736 (1.49%)	
occurrences (all)	9	13	
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 840 (0.36%)	6 / 736 (0.82%)	
occurrences (all)	3	6	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	10 / 840 (1.19%)	12 / 736 (1.63%)	
occurrences (all)	11	12	
Muscle spasticity			
subjects affected / exposed	9 / 840 (1.07%)	3 / 736 (0.41%)	
occurrences (all)	9	3	
Headache			
subjects affected / exposed	142 / 840 (16.90%)	131 / 736 (17.80%)	
occurrences (all)	303	242	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 840 (3.69%)	28 / 736 (3.80%)	
occurrences (all)	46	35	
Lymphopenia			
subjects affected / exposed	92 / 840 (10.95%)	83 / 736 (11.28%)	
occurrences (all)	125	108	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed occurrences (all)	15 / 840 (1.79%) 15	13 / 736 (1.77%) 18	
Gastritis subjects affected / exposed occurrences (all)	17 / 840 (2.02%) 17	15 / 736 (2.04%) 17	
Diarrhoea subjects affected / exposed occurrences (all)	37 / 840 (4.40%) 42	21 / 736 (2.85%) 26	
Haemorrhoids subjects affected / exposed occurrences (all)	9 / 840 (1.07%) 10	8 / 736 (1.09%) 8	
Vomiting subjects affected / exposed occurrences (all)	8 / 840 (0.95%) 9	5 / 736 (0.68%) 8	
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	6 / 840 (0.71%) 7	1 / 736 (0.14%) 1	
Dermatitis allergic subjects affected / exposed occurrences (all)	7 / 840 (0.83%) 7	5 / 736 (0.68%) 5	
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	7 / 840 (0.83%) 11	6 / 736 (0.82%) 7	
Nephrolithiasis subjects affected / exposed occurrences (all)	6 / 840 (0.71%) 6	2 / 736 (0.27%) 2	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	29 / 840 (3.45%) 31	26 / 736 (3.53%) 33	
Back pain subjects affected / exposed occurrences (all)	81 / 840 (9.64%) 99	72 / 736 (9.78%) 89	
Arthralgia			

subjects affected / exposed occurrences (all)	53 / 840 (6.31%) 61	43 / 736 (5.84%) 48	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	17 / 840 (2.02%)	13 / 736 (1.77%)	
occurrences (all)	19	13	
COVID-19			
subjects affected / exposed	130 / 840 (15.48%)	116 / 736 (15.76%)	
occurrences (all)	136	124	
Bronchitis			
subjects affected / exposed	58 / 840 (6.90%)	38 / 736 (5.16%)	
occurrences (all)	75	46	
Viral infection			
subjects affected / exposed	7 / 840 (0.83%)	7 / 736 (0.95%)	
occurrences (all)	9	8	
Urinary tract infection			
subjects affected / exposed	52 / 840 (6.19%)	48 / 736 (6.52%)	
occurrences (all)	106	75	
Upper respiratory tract infection			
subjects affected / exposed	101 / 840 (12.02%)	99 / 736 (13.45%)	
occurrences (all)	162	146	
Sinusitis			
subjects affected / exposed	33 / 840 (3.93%)	37 / 736 (5.03%)	
occurrences (all)	38	51	
Respiratory tract infection viral			
subjects affected / exposed	52 / 840 (6.19%)	46 / 736 (6.25%)	
occurrences (all)	91	68	
Respiratory tract infection			
subjects affected / exposed	56 / 840 (6.67%)	53 / 736 (7.20%)	
occurrences (all)	86	88	
Pharyngitis			
subjects affected / exposed	39 / 840 (4.64%)	30 / 736 (4.08%)	
occurrences (all)	49	37	
Nasopharyngitis			
subjects affected / exposed	176 / 840 (20.95%)	164 / 736 (22.28%)	
occurrences (all)	316	320	

Influenza subjects affected / exposed occurrences (all)	32 / 840 (3.81%) 40	24 / 736 (3.26%) 28	
Metabolism and nutrition disorders			
Dyslipidaemia subjects affected / exposed occurrences (all)	10 / 840 (1.19%) 10	15 / 736 (2.04%) 15	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	36 / 840 (4.29%) 37	32 / 736 (4.35%) 34	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported