



Clinical trial results:

Phase 2, Randomized, Multi-Center, Double-blind, Dose-ranging, Placebo-controlled, Adaptive Design Study to Evaluate the Efficacy and Safety/Pharmacokinetics of BMS-986142 in Subjects With Moderate to Severe Rheumatoid Arthritis with an Inadequate Response to Methotrexate with or without TNF Inhibitors

Summary

EudraCT number	2015-002887-17
Trial protocol	ES AT BE FR NL
Global end of trial date	03 May 2018

Results information

Result version number	v1 (current)
This version publication date	22 September 2019
First version publication date	22 September 2019

Trial information

Trial identification

Sponsor protocol code	IM006-016
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02638948
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb Study Director
Sponsor organisation address	3401 Princeton Pike, Lawrenceville, United States, NJ 08543
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb Study Director, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb Study Director, 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	03 May 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to compare the efficacy of BMS-986142 versus placebo on a background of methotrexate (MTX) as assessed by American College of Rheumatology (ACR)20 and ACR70 response rates at Week 12.

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2016
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	Argentina: 15
Country: Number of subjects enrolled	Brazil: 42
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Japan: 50
Country: Number of subjects enrolled	Mexico: 96
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Russian Federation: 44
Country: Number of subjects enrolled	South Africa: 61
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 152
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 4
Worldwide total number of subjects	508
EEA total number of subjects	36

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)	367
From 65 to 84 years	139
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 508 subjects who signed the informed consent form and were enrolled in the study; 248 subjects were randomized, and 247 subjects were administered study drug (1 subject decided after randomization to initiate treatment with a different medication instead).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Oral dose of matching placebo for BMS-986142 was administered daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Matching Placebo for BMS-986142
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose

Arm title	BMS 100mg
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Arm description:

Oral dose of BMS-986142 100mg was administered daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	BMS-986142
Investigational medicinal product code	BMS-986142-01
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose

Arm title	BMS 200mg
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Arm description:

Oral dose of BMS-986142 200mg was administered daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	BMS-986142
Investigational medicinal product code	BMS-986142-01
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose

Arm title	BMS 350mg
Arm description:	
Oral dose of BMS-986142 350mg was administered daily for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	BMS-986142
Investigational medicinal product code	BMS-986142-01
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose

Number of subjects in period 1^[1]	Placebo	BMS 100mg	BMS 200mg
Started	75	73	73
Completed	66	62	66
Not completed	9	11	7
Other than specified above	4	1	1
Consent withdrawn by subject	4	5	2
Poor/Non-Compliance	-	2	1
Adverse event, non-fatal	-	-	1
Lost to follow-up	-	-	1
Subject no longer meets study criteria	-	1	-
Administrative Reason by Sponsor	-	1	-
Subject requested to discontinue study treatment	-	-	1
Lack of efficacy	1	1	-

Number of subjects in period 1^[1]	BMS 350mg
Started	26
Completed	18
Not completed	8
Other than specified above	1
Consent withdrawn by subject	1
Poor/Non-Compliance	-
Adverse event, non-fatal	1
Lost to follow-up	1

Subject no longer meets study criteria	-
Administrative Reason by Sponsor	4
Subject requested to discontinue study treatment	-
Lack of efficacy	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 508 subjects who signed the informed consent form and were enrolled in the study; 248 subjects were randomized, and 247 subjects were administered study drug.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Oral dose of matching placebo for BMS-986142 was administered daily for 12 weeks.	
Reporting group title	BMS 100mg
Reporting group description:	
Oral dose of BMS-986142 100mg was administered daily for 12 weeks.	
Reporting group title	BMS 200mg
Reporting group description:	
Oral dose of BMS-986142 200mg was administered daily for 12 weeks.	
Reporting group title	BMS 350mg
Reporting group description:	
Oral dose of BMS-986142 350mg was administered daily for 12 weeks.	

Reporting group values	Placebo	BMS 100mg	BMS 200mg
Number of subjects	75	73	73
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	51	51	57
From 65-84 years	24	22	16
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	58.6	57.6	55.2
standard deviation	± 11.61	± 13.01	± 13.13
Sex: Female, Male Units: Subjects			
Female	64	67	62
Male	11	6	11
Race/Ethnicity, Customized Units: Subjects			
White	52	54	58
Black or African American	6	9	5
Asian	14	8	8
Other	3	2	2
Ethnicity Units: Subjects			
Hispanic or Latino	22	24	28
Not Hispanic or Latino	27	24	25

Unknown or Not Reported	26	25	20
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Reporting group values	BMS 350mg	Total	
Number of subjects	26	247	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	21	180	
From 65-84 years	5	67	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	52.9		
standard deviation	± 13.16	-	
Sex: Female, Male Units: Subjects			
Female	21	214	
Male	5	33	
Race/Ethnicity, Customized Units: Subjects			
White	24	188	
Black or African American	1	21	
Asian	1	31	
Other	0	7	
Ethnicity Units: Subjects			
Hispanic or Latino	10	84	
Not Hispanic or Latino	8	84	
Unknown or Not Reported	8	79	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Oral dose of matching placebo for BMS-986142 was administered daily for 12 weeks.	
Reporting group title	BMS 100mg
Reporting group description:	
Oral dose of BMS-986142 100mg was administered daily for 12 weeks.	
Reporting group title	BMS 200mg
Reporting group description:	
Oral dose of BMS-986142 200mg was administered daily for 12 weeks.	
Reporting group title	BMS 350mg
Reporting group description:	
Oral dose of BMS-986142 350mg was administered daily for 12 weeks.	

Primary: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 12
End point description:	
ACR responses are assessed with a composite rating scale of the American College of Rheumatology that includes 7 variables: tender joint count (TJC); swollen joint count (SJC); levels of an acute phase reactant C-reactive Protein levels (CRP); participant's assessment of pain; participant's global assessment of disease activity; physician's global assessment of disease activity; participant's assessment of physical function by health assessment questionnaire disability index (HAQ-DI). ACR20 is defined as achieving at least 20% improvement in both TJC and SJC, and at least 20% improvement in at least 3 of the 5 other assessments of the ACR. Analysis was performed on efficacy population which excluded subjects who were randomized to a treatment arm and discontinued based on the interim analysis (IA).	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving ACR20 Response at Week 12	30.7 (20.2 to 41.1)	35.6 (24.6 to 46.6)	42.5 (31.1 to 53.8)	30.8 (13.0 to 48.5)

Statistical analyses

Statistical analysis title	BMS-986142 100 mg vs Placebo
Comparison groups	Placebo v BMS 100mg

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5224 ^[1]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	20.1

Notes:

[1] - Threshold for significance = 0.05

Statistical analysis title	BMS-986142 200 mg vs Placebo
Comparison groups	Placebo v BMS 200mg
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.136 ^[2]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	27.2

Notes:

[2] - Threshold for significance = 0.05

Statistical analysis title	BMS-986142 350 mg vs Placebo
Comparison groups	Placebo v BMS 350mg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9922 ^[3]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.5
upper limit	20.7

Notes:

[3] - Threshold for significance = 0.05

Primary: Percentage of Subjects Achieving American College of Rheumatology 70%

(ACR70) Response at Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 70% (ACR70) Response at Week 12
End point description:	
ACR responses are assessed with a composite rating scale of the American College of Rheumatology that includes 7 variables: TJC; SJC; levels of an acute phase reactant (CRP level); participant' assessment of pain; participant's global assessment of disease activity; physician's global assessment of disease activity; participant's assessment of physical function by HAQ--DI. ACR70 is defined as achieving at least 70% improvement in both TJC and SJC, and at least 70% improvement in at least 3 of the 5 other assessments of the ACR. Analysis was performed on efficacy population.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving ACR70 Response at Week 12	4.0 (0.8 to 11.2)	4.1 (0.9 to 11.5)	9.6 (2.8 to 16.3)	3.8 (0.1 to 19.6)

Statistical analyses

Statistical analysis title	BMS-986142 100 mg vs Placebo
Comparison groups	Placebo v BMS 100mg
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 1 ^[4]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	16.5

Notes:

[4] - Threshold for significance = 0.05

Statistical analysis title	BMS-986142 200 mg vs Placebo
Comparison groups	Placebo v BMS 200mg

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2058 ^[5]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.5
upper limit	21.9

Notes:

[5] - Threshold for significance = 0.05

Statistical analysis title	BMS-986142 350 mg vs Placebo
Comparison groups	Placebo v BMS 350mg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 1 ^[6]
Method	Chi-squared
Parameter estimate	Estimate of Difference (%)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.5
upper limit	22.2

Notes:

[6] - Threshold for significance = 0.05

Secondary: Percentage of Subjects Achieving American College of Rheumatology 20% Response Over Time From Baseline to Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 20% Response Over Time From Baseline to Week 12
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End point description:

ACR responses are assessed with a composite rating scale of the American College of Rheumatology that includes 7 variables: tender joint count (TJC); swollen joint count (SJC); levels of an acute phase reactant C-reactive Protein levels (CRP); participant's assessment of pain; participant's global assessment of disease activity; physician's global assessment of disease activity; participant's assessment of physical function by health assessment questionnaire disability index (HAQ-DI). ACR20 is defined as achieving at least 20% improvement in both TJC and SJC, and at least 20% improvement in at least 3 of the 5 other assessments of the ACR. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Up to Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 15	10.7 (3.7 to 17.7)	13.7 (5.8 to 21.6)	24.7 (14.8 to 34.5)	15.4 (4.4 to 34.9)
Day 29	18.7 (9.8 to 27.5)	23.3 (13.6 to 33)	21.9 (12.4 to 31.4)	26.9 (9.9 to 44)
Day 57	28 (17.8 to 38.2)	41.1 (29.8 to 52.4)	39.7 (28.5 to 51)	15.4 (4.4 to 34.9)
Day 87	30.7 (20.2 to 41.1)	35.6 (24.6 to 46.6)	42.5 (31.1 to 53.8)	30.8 (13 to 48.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 50% (ACR50) Response at Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 50% (ACR50) Response at Week 12
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End point description:

ACR responses are assessed with a composite rating scale of the American College of Rheumatology that includes 7 variables: TJC; SJC; levels of an acute phase reactant (CRP level); subject's assessment of pain; subject's global assessment of disease activity; physician's global assessment of disease activity; subject's assessment of physical function by HAQ--DI. ACR70 is defined as achieving at least 50% improvement in both TJC and SJC, and at least 50% improvement in at least 3 of the 5 other assessments of the ACR. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Up to Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 15	2.7 (0.3 to 9.3)	4.1 (0.9 to 11.5)	5.5 (1.5 to 13.4)	3.8 (0.1 to 19.6)
Day 29	2.7 (0.3 to 9.3)	4.1 (0.9 to 11.5)	6.8 (1.1 to 12.6)	7.7 (0.9 to 25.1)
Day 57	9.3 (2.7 to 15.9)	12.3 (4.8 to 19.9)	13.7 (5.8 to 21.6)	7.7 (0.9 to 25.1)
Day 85	9.3 (2.7 to 15.9)	13.7 (5.8 to 21.6)	16.4 (7.9 to 24.9)	11.5 (2.4 to 30.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 70% Response Over Time From Baseline to Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 70% Response Over Time From Baseline to Week 12
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End point description:

CR responses are assessed with a composite rating scale of the American College of Rheumatology that includes 7 variables: TJC; SJC; levels of an acute phase reactant (CRP level); participant's assessment of pain; participant's global assessment of disease activity; physician's global assessment of disease activity; participant's assessment of physical function by HAQ--DI. ACR70 is defined as achieving at least 70% improvement in both TJC and SJC, and at least 70% improvement in at least 3 of the 5 other assessments of the ACR. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Up to Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 15	1.3 (0 to 7.2)	0 (0 to 4.9)	1.4 (0 to 7.4)	0 (0 to 13.2)
Day 29	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Day 57	1.3 (0 to 7.2)	5.5 (1.5 to 13.4)	5 (1.5 to 13.4)	3.8 (0.1 to 19.6)
Day 85	4 (0.8 to 11.2)	4.1 (0.9 to 11.5)	9.6 (2.8 to 16.3)	3.8 (0.1 to 19.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving < 2.6 Response in Disease Activity Score for 28 Joints -C-Reactive Protein (DAS28--CRP) Score at Week 12

End point title	Percentage of Subjects Achieving < 2.6 Response in Disease Activity Score for 28 Joints -C-Reactive Protein (DAS28--CRP) Score at Week 12
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End point description:

DAS28 is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); General health (GH) assessment by the subjects assessed from the ACR rheumatoid arthritis (RA) core set questionnaire (participant global assessment) in 100 mm visual analog scale (VAS). Marker of inflammation assessed by the high sensitivity C-reactive protein (hs-CRP) in mg/L. The DAS28 score provides a number indicating the current disease activity of the RA. DAS28 total score ranges from 2-10. A DAS28 score above 5.1 means high disease activity, whereas a DAS28 score below 3.2 indicates low disease activity and a DAS28 score below 2.6 means disease remission. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving < 2.6 in DAS28-CRP Score	6.7 (1.0 to 12.3)	9.6 (2.8 to 16.3)	11.0 (3.8 to 18.1)	0.0 (0.0 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving < 2.6 Response in Disease Activity Score for 28 Joints Erythrocyte Sedimentation Rate (DAS28--ESR) Score at Week 12

End point title	Percentage of Subjects Achieving < 2.6 Response in Disease Activity Score for 28 Joints Erythrocyte Sedimentation Rate (DAS28--ESR) Score at Week 12
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End point description:

DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); General health (GH) assessment by the subject assessed from the ACR RA core set questionnaire (participant global assessment) in 100 mm VAS; Marker of inflammation assessed by ESR in mm/hr. The DAS28-ESR score provides a number indicating the current disease activity of the RA. DAS28-ESR total score ranges from 2-10. A DAS28-ESR score above 5.1 means high disease activity, DAS28-ESR score below 3.2 indicates low disease activity and DAS28-ESR score below 2.6 means disease remission. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving < 2.6 in DAS28--ESR Score	0.0 (0.0 to 4.8)	6.8 (1.1 to 12.6)	1.4 (0.0 to 7.4)	0.0 (0.0 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving ≤ 2.8 Response in Clinical Disease Activity Index (CDAI) Score at Week 12

End point title	Percentage of Subjects Achieving ≤ 2.8 Response in Clinical Disease Activity Index (CDAI) Score at Week 12
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End point description:

CDAI is a composite index constructed to measure clinical remission in RA that does not include a laboratory test, and is a numerical summation of 4 components: TJC (28 joints), SJC (28 joints), Participant's Global Assessment of Disease Activity VAS (in cm), and Physician's Global Assessment of Disease VAS (in cm). Total scores ranges from 0 to 76 with a negative change in CDAI score indicating an improvement in disease activity and a positive change in score indicating a worsening of disease activity. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving ≤ 2.8 in CDAI Score	0.0 (0.0 to 4.8)	6.8 (1.1 to 12.6)	6.8 (1.1 to 12.6)	0.0 (0.0 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving ≤ 3.3 Response in Simple Disease Activity Index (SDAI) Score at Week 12

End point title	Percentage of Subjects Achieving ≤ 3.3 Response in Simple Disease Activity Index (SDAI) Score at Week 12
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End point description:

The SDAI is the numerical sum of five outcome parameters: TJC and SJC based on a 28-joint assessment, patient global assessment (PtGA) and physician global assessment (PGA) assessed on a VAS scale ranging from 0 to 10 cm, where higher scores indicate greater affection due to disease activity, and CRP measured in terms of milligram per deciliter (mg/dL). SDAI total score ranges from 0 to 86. SDAI ≤ 3.3 indicates disease remission, > 3.4 to 11 indicates low disease activity, >11 to 26 indicates moderate disease activity, and >26 indicates high disease activity. Analysis was performed on efficacy population.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving ≤ 3.3 in SDAI Score	0.0 (0.0 to 4.8)	6.8 (1.1 to 12.6)	6.8 (1.1 to 12.6)	0.0 (0.0 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Boolean Remission Criteria at Week 12

End point title	Percentage of Subjects Achieving Boolean Remission Criteria at Week 12
End point description: Boolean remission criteria was defined as: TJC28 ≤ 1 ; SJC28 ≤ 1 ; physician's global assessment ≤ 1 ; and CRP ≤ 1 mg/dL. Analysis was performed on efficacy population.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Percentage of Subjects				
number (confidence interval 95%)				
% of Subjects Achieving Boolean Remission Criteria	1.3 (0.0 to 7.2)	4.1 (0.9 to 11.5)	4.1 (0.9 to 11.5)	0.0 (0.0 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in DAS28-CRP Score Over Time up to Week 12

End point title	Change From Baseline in DAS28-CRP Score Over Time up to Week 12
End point description: DAS28 is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); General health (GH) assessment by the subject assessed from the ACR rheumatoid arthritis (RA) core set questionnaire (participant global assessment) in 100 mm visual analog scale (VAS). Marker of inflammation assessed by the high sensitivity C-reactive protein (hs-CRP) in mg/L. The DAS28 score provides a number indicating the current disease activity of the RA. DAS28 total score ranges from 2-10. A DAS28 score above 5.1 means high disease activity, whereas a DAS28 score below 3.2 indicates low disease activity and a DAS28 score below 2.6 means disease remission. Analysis was performed on efficacy population. Here 'N' signifies number of subjects analyzed who were evaluable for this outcome measure.	

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	64	15
Units: Units on a scale				
arithmetic mean (standard error)				
CFB in DAS28-CRP Score Over Time up to Week 12	-1.1 ($\pm$ 0.141)	-1.1 ($\pm$ 0.176)	-1.4 ($\pm$ 0.168)	-1.4 ($\pm$ 0.194)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in DAS28-ESR Score Over Time up to Week 12

End point title	Change From Baseline in DAS28-ESR Score Over Time up to Week 12
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End point description:

DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); General health (GH) assessment by the subject assessed from the ACR RA core set questionnaire (participant global assessment) in 100 mm VAS; Marker of inflammation assessed by ESR in mm/hr. The DAS28-ESR score provides a number indicating the current disease activity of the RA. DAS28-ESR total score ranges from 2-10. A DAS28-ESR score above 5.1 means high disease activity, DAS28-ESR score below 3.2 indicates low disease activity and DAS28-ESR score below 2.6 means disease remission. Analysis was performed on efficacy population. Here 'N' signifies number of subjects analyzed who were evaluable for this outcome measure.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	65	14
Units: Units on a scale				
arithmetic mean (standard error)				
CFB in DAS28-ESR Score Over Time up to Week 12	-1.1 ($\pm$ 0.149)	-1.1 ($\pm$ 0.166)	-1.4 ($\pm$ 0.161)	-1.5 ($\pm$ 0.247)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CDAI Score Over Time up to Week 12

End point title	Change From Baseline in CDAI Score Over Time up to Week 12
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End point description:

CDAI is a composite index constructed to measure clinical remission in RA that does not include a laboratory test, and is a numerical summation of 4 components: TJC (28 joints), SJC (28 joints), Participant's Global Assessment of Disease Activity VAS (in cm), and Physician's Global Assessment of Disease VAS (in cm). Total scores ranges from 0 to 76 with a negative change in CDAI score indicating an improvement in disease activity and a positive change in score indicating a worsening of disease activity. Analysis was performed on efficacy population. Here 'N' signifies number of subjects analyzed who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	61	68	16
Units: Units on a scale				
arithmetic mean (standard error)				
CFB in CDAI Score Over Time up to Week 12	-14.9 (± 1.591)	-13.6 (± 2.030)	-16 (± 1.828)	-17.6 (± 2.519)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in SDAI Score Over Time up to Week 12

End point title	Change From Baseline in SDAI Score Over Time up to Week 12
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End point description:

The SDAI is the numerical sum of five outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on a VAS scale ranging from 0 to 10 cm, where higher scores indicate greater affection due to disease activity, and CRP measured in terms of mg/dL. SDAI total score ranges from 0 to 86. SDAI ≤ 3.3 indicates disease remission, > 3.4 to 11 indicates low disease activity, >11 to 26 indicates moderate disease activity, and >26 indicates high disease activity. Analysis was performed on efficacy population. Here 'N' signifies number of subjects analyzed who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	61	64	15
Units: Units on a scale				
arithmetic mean (standard error)				

CFB in SDAI Score Over Time up to Week 12	-14.8 (± 1.628)	-13.9 (± 2.090)	-16.6 (± 1.954)	-18.9 (± 3.218)
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs), and Serious AEs (SAEs)

End point title	Number of Subjects With Adverse Events (AEs), and Serious AEs (SAEs)
End point description: An AE is any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An AE can therefore be any unfavorable and unintended sign (example, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death, initial or prolonged inpatient hospitalization, life-threatening experience (immediate risk of dying), persistent or significant disability/incapacity, or a congenital anomaly, or a medically important event. Analysis was performed on all treated subjects.	
End point type	Secondary
End point timeframe: Up to 30 days after treatment discontinuation	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Subjects				
AEs	36	39	39	19
SAEs	4	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Observed Plasma Concentration (C_{trough}) of BMS-986142

End point title	Trough Observed Plasma Concentration (C _{trough}) of BMS-986142 ^[7]
End point description: C _{trough} was defined as trough observed plasma concentration. Analysis was performed on pharmacokinetic population which included all subjects who received BMS-986142 and had any available concentration-time data.	
End point type	Secondary
End point timeframe: Week 4, 8, and 12	

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point evaluated PK characteristic for Experimental Arms only.

End point values	BMS 100mg	BMS 200mg	BMS 350mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	73	26	
Units: nanogram/mL				
geometric mean (geometric coefficient of variation)				
Week 4	47.9 (± 119.0)	111.8 (± 101.7)	195.9 (± 91.9)	
Week 8	41.2 (± 95.3)	92.2 (± 124.5)	283.0 (± 133.3)	
Week 12	28.4 (± 123.0)	75.6 (± 155.4)	169.5 (± 83.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Synovitis at Week 4 and 12

End point title	Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Synovitis at Week 4 and 12
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End point description:

ynovitis is assessed in 3 wrist regions (A. the distal radioulnar joint; B. the radiocarpal joint; C. the intercarpal and carpometacarpophalangeal, CMC, joints) and in each MCP joint. For each wrist region, possible score ranges from 0–3, with 0=normal, 1=mild, 2=moderate, and 3=severe damage. The total synovitis score per wrist=the sum of the individual scores for the 3 wrist regions. Minimum score per wrist ranges from 0, indicating no damage, to 9 (score of 3*3 wrist regions), indicating most severe damage. A negative change from baseline indicates improvement.

End point type	Secondary
End point timeframe:	
Week 4 and Week 12	

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4 (n = 68,66,70,23)	0.1 (± 0.226)	-0.2 (± 0.202)	0.1 (± 0.182)	0.1 (± 0.558)
Week 12 (n = 68,66,70,23)	0.7 (± 0.467)	-0.0 (± 0.315)	-0.3 (± 0.263)	0.9 (± 1.163)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Osteitis at Weeks 4 and 12

End point title	Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Osteitis at Weeks 4 and 12
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End point description:

Osteitis was assessed at a total of 23 anatomic locations: 15 in 1 wrist and 8 in the hand of the same side. Each site is scored in 1.0 increments from 0 to 3, indicating involvement of original articular bone. The total score for the hands/wrists is the sum of the individual scores for each location. Thus the maximum score achievable per hand/wrist is 23 (total number of anatomic locations) * 3 (maximum per joint)=69. Minimum score=0, indicating normal. Increasing score=greater severity. A negative change from baseline indicates improvement.

End point type	Secondary
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End point timeframe:

Week 4 and Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4 (n = 64, 65, 69, 22)	0.1 (± 0.223)	0.2 (± 0.262)	0.1 (± 0.148)	-0.1 (± 0.249)
Week 12 (n = 64, 65, 69, 22)	0.4 (± 0.574)	0.5 (± 0.451)	0.0 (± 0.257)	0.2 (± 0.654)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Bone Erosion at Weeks 4 and 12

End point title	Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Bone Erosion at Weeks 4 and 12
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End point description:

Bone erosion assessed at a total of 23 anatomic locations: 15 in 1 wrist and 8 in the hand of the same side. Each site is scored in 1.0 increments from 0 (no damage) to 10 (severe damage) according to erosion of the original articular bone (each unit=10% loss of articular bone). The total erosion score for the hands/wrists is the sum of the individual scores for each location. Thus the maximum score achievable per hand/wrist is 230. Increasing score=greater severity. A negative change from baseline indicates improvement.

End point type	Secondary
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End point timeframe:

Week 4 and Week 12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4 (n = 69, 67, 70, 23)	0.1 (± 0.048)	0.1 (± 0.089)	-0.0 (± 0.036)	0.0 (± 0.030)
Week 12 (n = 69, 67, 70, 23)	0.1 (± 0.048)	0.3 (± 0.248)	0.0 (± 0.046)	0.1 (± 0.072)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Cartilage Loss at Weeks 4 and 12

End point title	Mean Change from Baseline in Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS) scores for Cartilage Loss at Weeks 4 and 12
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End point description:

Cartilage loss was assessed by MRI. Scans of 25 joints were read and scored for each participant by assessors. Scores for each location ranged 0-4 on a 9-point scale, with 0= no cartilage loss and 4= complete cartilage loss. Total score was the sum of the 25 individual scores and ranged 0-100 with 0= no cartilage loss and 100= most severe cartilage loss. A negative change from baseline indicates improvement.

End point type	Secondary
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End point timeframe:

Week 4 and week12

End point values	Placebo	BMS 100mg	BMS 200mg	BMS 350mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	73	73	26
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4 (n = 69, 67, 70, 23)	0.1 (± 0.105)	0.0 (± 0.064)	-0.0 (± 0.079)	0.4 (± 0.169)
Week 12 (n = 69, 67, 70, 23)	0.0 (± 0.116)	0.3 (± 0.139)	0.0 (± 0.111)	0.5 (± 0.294)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events were collected from signature of the informed consent until 30 days after last treatment administration (Approximately 26 months)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Oral dose of matching placebo for BMS-986142 was administered daily for 12 weeks.

Reporting group title	BMS 100 mg
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Reporting group description:

Oral dose of BMS-986142 100 milligram (mg) was administered daily for 12 weeks.

Reporting group title	BMS 200 mg
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Reporting group description:

Oral dose of BMS-986142 200 mg was administered daily for 12 weeks.

Reporting group title	BMS 350 mg
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Reporting group description:

Oral dose of BMS-986142 350 mg was administered daily for 12 weeks.

Serious adverse events	Placebo	BMS 100 mg	BMS 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 75 (5.33%)	2 / 73 (2.74%)	0 / 73 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 73 (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
Injury, poisoning and procedural complications			
Open globe injury			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 73 (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
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 73 (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
Mouth ulceration			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 73 (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
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 73 (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

Serious adverse events	BMS 350 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Open globe injury			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Angina pectoris subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 26 (0.00%) 0 / 0 0 / 0		
Gastrointestinal disorders Intestinal obstruction subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 26 (0.00%) 0 / 0 0 / 0		
Mouth ulceration subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 26 (0.00%) 0 / 0 0 / 0		
Musculoskeletal and connective tissue disorders Rheumatoid arthritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 26 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	Placebo	BMS 100 mg	BMS 200 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 75 (14.67%)	12 / 73 (16.44%)	16 / 73 (21.92%)
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 4	0 / 73 (0.00%) 0	1 / 73 (1.37%) 1
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	2 / 75 (2.67%) 2	0 / 73 (0.00%) 0	1 / 73 (1.37%) 1
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 73 (0.00%) 0
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	2 / 75 (2.67%) 2	2 / 73 (2.74%) 2	4 / 73 (5.48%) 4
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 75 (1.33%) 1	1 / 73 (1.37%) 1	3 / 73 (4.11%) 3
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	2 / 75 (2.67%) 2 1 / 75 (1.33%) 2	4 / 73 (5.48%) 4 5 / 73 (6.85%) 5	3 / 73 (4.11%) 4 5 / 73 (6.85%) 7
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 3	1 / 73 (1.37%) 1	3 / 73 (4.11%) 4

Non-serious adverse events	BMS 350 mg		
Total subjects affected by non-serious adverse events subjects affected / exposed	14 / 26 (53.85%)		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 6 2 / 26 (7.69%) 2 4 / 26 (15.38%) 7		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	5 / 26 (19.23%) 5		
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all)	6 / 26 (23.08%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2016	Incorporate changes in response to health authorities' comments and update information collected during course of study.
04 August 2016	Introduced a change in ratio of the subpopulation of patients with RA from predominantly tumor necrosis factor- inadequate responder(s) (TNF-IR) to predominantly MTX-IR.
29 October 2017	- This protocol was updated mainly to incorporate preliminary results of drug-drug interactions studies IM006-031 and IM006-032 as described in Dear Investigator Letter dated 17-Oct-2016. - Revisions were also made to provide further clarifications on study timelines, leflunomide washout, inclusion and exclusion criteria, PI expectations on x-ray and MRI results, Physicians Global Assessment of Disease Activity (PGA) and Joint Count Assessments, as well as to include administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported