Clinical trial results:
Randomized, double-blind, placebo-controlled, multicenter, phase IIb dose finding study of GLPG0634 administered for 24 weeks in combination with methotrexate to subjects with moderately to severely active rheumatoid arthritis who have an inadequate response to methotrexate alone

Summary

EudraCT number	2012-003635-31
Trial protocol	BE HU DE CZ ES AT LV BG
Global end of trial date	14 May 2015

Results information

Result version number	v1 (current)
This version publication date	29 May 2016
First version publication date	29 May 2016

Trial information

Trial identification

Sponsor protocol code	GLPG0634-CL-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01888874
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos N.V.
Sponsor organisation address	Generaal De Wittelaan L11 A3, 2800, Mechelen, Belgium,
Public contact	Clinical Trial Information Desk, Galapagos N.V., +32 (0)15 342 900, rd@glpg.com
Scientific contact	Clinical Trial Information Desk, Galapagos N.V., +32 (0)15 342 900, rd@glpg.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	14 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy in terms of the percentage of subjects achieving an American College of Rheumatology (ACR)20 response, of different doses and dose regimens of GLPG0634 compared to placebo at Week 12.

Protection of trial subjects:

Before initiation of the study at each study center, the protocol, the informed consent form (ICF), other written material given to the subjects, and any other relevant study documentation was to be submitted to the appropriate IEC/IRB. Written approval of the study and all relevant study information was to be obtained before the study center could be initiated or the study medication was released to the investigator. Any necessary extensions or renewals of IEC/IRB approval were to be obtained for changes to the study such as modification of the protocol, the ICF or other study documentation. The written approval of the IEC/IRB together with the approved ICF was to be filed in the study files.

The investigator was to promptly report to the IEC/IRB any new information that could have adversely affected the safety of the subjects or the conduct of the study. The investigator was to submit written summaries of the study status to the IEC/IRB as required. On completion of the study, the IEC/IRB was to be notified that the study had ended.

Background therapy:

Methotrexate (MTX) was the standard background therapy for this study.

Evidence for comparator: -

Actual start date of recruitment	17 July 2013
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	Poland: 59
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bulgaria: 33
Country: Number of subjects enrolled	Czech Republic: 18
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 36
Country: Number of subjects enrolled	Latvia: 26
Country: Number of subjects enrolled	Argentina: 59
Country: Number of subjects enrolled	Mexico: 57
Country: Number of subjects enrolled	Chile: 36

Country: Number of subjects enrolled	Colombia: 36
Country: Number of subjects enrolled	Guatemala: 34
Country: Number of subjects enrolled	Russian Federation: 45
Country: Number of subjects enrolled	Ukraine: 36
Country: Number of subjects enrolled	Moldova, Republic of: 16
Country: Number of subjects enrolled	United States: 72
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Israel: 5
Worldwide total number of subjects	599
EEA total number of subjects	191

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)	499
From 65 to 84 years	100
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe, South America, North America, Australia, and New Zealand. The first participant was screened on17 July 2013. The last study visit occurred on 14 May 2015.

Pre-assignment

Screening details:

1255 subjects were screened.

Period 1

Period 1 title	Period 1: Weeks 1 - 12
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:

Placebo during Weeks 1 - 12; responders (having at least 20% improvement on TJC68 and SJC66) remained on placebo while nonresponders were re-randomized to 100 mg QD or 50 mg BID during Weeks 13-24

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

Dosage and administration details:

2 placebo capsules both in the morning and in the evening

Arm title	GLPG0634 50 mg QD

Arm description:

GLPG0634 50 mg once daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 100 mg QD during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule in the morning and 2 placebo capsules in the evening

Arm title	GLPG0634 100 mg QD
Arm description:	
GLPG0634 100 mg once daily + placebo during Weeks 1-24	
Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1 GLPG0634 100 mg capsule once daily in the morning	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1 placebo capsule in the morning and 2 placebo capsules in the evening	
Arm title	GLPG0634 200 mg QD
Arm description:	
GLPG0634 200 mg once daily + placebo during Weeks 1-24	
Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
2 GLPG0634 100 mg capsules once daily in the morning	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
2 placebo capsules in the evening	
Arm title	GLPG0634 25 mg BID
Arm description:	
GLPG0634 25 mg twice daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 50 mg BID during Weeks 13-24	
Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1 GLPG0634 25 mg capsule twice daily in the morning and in the evening	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	GLPG0634 50 mg BID

Arm description:

GLPG0634 50 mg twice daily + placebo during Weeks 1-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	GLPG0634 100 mg BID

Arm description:

GLPG0634 100 mg twice daily + placebo during Weeks 1-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 100 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Number of subjects in period 1[1]	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD
Started	86	82	85
Completed	83	76	78
Not completed	3	6	7
Non-compliance with the study procedures	-	1	-
Withdrawal of the subject's consent	2	-	-
Withdrawal of the subject’s consent	-	2	3
Adverse event, non-fatal	-	2	3
Other	1	-	1
AE and treatment failure	-	-	-
Investigator’s decision	-	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1[1]	GLPG0634 200 mg QD	GLPG0634 25 mg BID	GLPG0634 50 mg BID
Started	86	86	85
Completed	80	77	80
Not completed	6	9	5
Non-compliance with the study procedures	-	-	-
Withdrawal of the subject's consent	-	-	-
Withdrawal of the subject’s consent	4	3	-
Adverse event, non-fatal	1	2	1
Other	1	3	3
AE and treatment failure	-	1	-
Investigator’s decision	-	-	-
Lost to follow-up	-	-	1

Number of subjects in period 1[1]	GLPG0634 100 mg BID
Started	84
Completed	83
Not completed	1
Non-compliance with the study procedures	-
Withdrawal of the subject's consent	-
Withdrawal of the subject’s consent	-
Adverse event, non-fatal	-
Other	-
AE and treatment failure	-
Investigator’s decision	1
Lost to follow-up	-

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: 5 subjects who were randomized but not treated are not included in the subject disposition table.

Period 2

Period 2 title	Period 2: Weeks 13 - 24
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Responders

Arm description:

Placebo during Weeks 1 - 12; responders remained on placebo during Weeks 13-24

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

Dosage and administration details:

2 placebo capsules twice daily in the morning and in the evening

Arm title	GLPG0634 50 mg QD Responders

Arm description:

GLPG0634 50 mg once daily + placebo during Weeks 1-12; responders remained on the same treatment during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule in the morning and 2 placebo capsules in the evening

Arm title	GLPG0634 25 mg BID Responders

Arm description:

GLPG0634 25 mg twice daily + placebo during Weeks 1-12; responders remained on the same treatment during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 25 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	Placebo Switch to GLPG0634 100 mg QD

Arm description:

Some nonresponders from the placebo group were re-randomized to receive GLPG0634 100 mg once daily + placebo during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 100 mg capsule once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule in the morning and 2 placebo capsules in the evening

Arm title	Placebo Switch to GLPG0634 50 mg BID

Arm description:

Some nonresponders from the placebo group were re-randomized to receive GLPG0634 50 mg twice daily + placebo during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	50 mg QD Switch to GLPG0634 100 mg QD

Arm description:

Nonresponders from the 50 mg QD group were re-randomized to receive GLPG0634 100 mg once daily + placebo during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 100 mg capsule once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule in the morning and 2 placebo capsules in the evening

Arm title	25 mg BID Switch to GLPG0634 50 mg BID

Arm description:

Nonresponders from the 25 mg BID group were re-randomized to receive GLPG0634 50 mg twice daily + placebo during Weeks 13-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	GLPG0634 100 mg QD

Arm description:

GLPG0634 100 mg once daily + placebo during Weeks 1-24

Arm type	Experimental

Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 100 mg capsule once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule in the morning and 2 placebo capsules in the evening

Arm title	GLPG0634 200 mg QD

Arm description:

GLPG0634 200 mg once daily + placebo during Weeks 1-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2 GLPG0634 100 mg capsules once daily in the morning

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2 placebo capsules in the evening

Arm title	GLPG0634 50 mg BID

Arm description:

GLPG0634 50 mg twice daily + placebo during Weeks 1-24

Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 50 mg capsule twice daily in the morning and in the evening

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 placebo capsule twice daily in the morning and in the evening

Arm title	GLPG0634 100 mg BID

Arm description:	
GLPG0634 100 mg twice daily + placebo during Weeks 1-24	
Arm type	Experimental
Investigational medicinal product name	GLPG0634
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1 GLPG0634 100 mg capsule twice daily in the morning and in the evening	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1 placebo capsule twice daily in the morning and in the evening	

Number of subjects in period 2	Placebo Responders	GLPG0634 50 mg QD Responders	GLPG0634 25 mg BID Responders
Started	53	57	60
Completed	50	55	57
Not completed	3	2	3
Withdrawal of the subject's consent	1	1	1
Treatment failure	-	-	-
Adverse event, non-fatal	2	-	1
Lost to follow-up	-	1	-
Adverse event and treatment failure	-	-	1
Non compliance with study medication	-	-	-

Number of subjects in period 2	Placebo Switch to GLPG0634 100 mg QD	Placebo Switch to GLPG0634 50 mg BID	50 mg QD Switch to GLPG0634 100 mg QD
Started	15	15	19
Completed	15	15	19
Not completed	0	0	0
Withdrawal of the subject's consent	-	-	-
Treatment failure	-	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-
Adverse event and treatment failure	-	-	-
Non compliance with study medication	-	-	-

Number of subjects in period 2	25 mg BID Switch to GLPG0634 50 mg BID	GLPG0634 100 mg QD	GLPG0634 200 mg QD

Started	17	78	80
Completed	17	70	78
Not completed	0	8	2
Withdrawal of the subject's consent	-	2	-
Treatment failure	-	1	-
Adverse event, non-fatal	-	3	2
Lost to follow-up	-	-	-
Adverse event and treatment failure	-	-	-
Non compliance with study medication	-	2	-

Number of subjects in period 2	GLPG0634 50 mg BID	GLPG0634 100 mg BID
Started	80	83
Completed	77	80
Not completed	3	3
Withdrawal of the subject's consent	-	-
Treatment failure	-	-
Adverse event, non-fatal	1	3
Lost to follow-up	1	-
Adverse event and treatment failure	-	-
Non compliance with study medication	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo during Weeks 1 - 12; responders (having at least 20% improvement on TJC68 and SJC66) remained on placebo while nonresponders were re-randomized to 100 mg QD or 50 mg BID during Weeks 13-24	
Reporting group title	GLPG0634 50 mg QD
Reporting group description:	
GLPG0634 50 mg once daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 100 mg QD during Weeks 13-24	
Reporting group title	GLPG0634 100 mg QD
Reporting group description:	
GLPG0634 100 mg once daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 200 mg QD
Reporting group description:	
GLPG0634 200 mg once daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 25 mg BID
Reporting group description:	
GLPG0634 25 mg twice daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 50 mg BID during Weeks 13-24	
Reporting group title	GLPG0634 50 mg BID
Reporting group description:	
GLPG0634 50 mg twice daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 100 mg BID
Reporting group description:	
GLPG0634 100 mg twice daily + placebo during Weeks 1-24	

Reporting group values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD
Number of subjects	86	82	85
Age categorical Units: Subjects			
< 45	20	20	22
≥ 45 to < 65	55	47	51
≥ 65 to < 75	9	14	8
≥ 75	2	1	4
Age continuous Units: years			
arithmetic mean	52	52.8	52.3
full range (min-max)	18 to 84	20 to 77	20 to 79
Gender categorical Units: Subjects			
Female	70	69	65
Male	16	13	20
Race Units: Subjects			
White	59	61	62
Other	26	21	22
Black or African American	1	0	0

Asian	0	0	1

RA duration			
Units: years			
arithmetic mean	8.21	7.21	7.67
full range (min-max)	0.5 to 36.5	0.6 to 21.3	0.6 to 32.6
C-reactive protein (CRP) at Baseline			
Units: mg/L			
arithmetic mean	16.25	27.71	24.54
full range (min-max)	1 to 84.5	1 to 158.7	1 to 140.7
Corrected tender joint count based on 68 joints (TJC68) at Baseline			
68 joints were assessed for tenderness and joints are classified as tender/not tender giving a total possible tender joint count score of 0 to 68.			
Units: units on a scale			
arithmetic mean	24.984	24.907	25.319
full range (min-max)	8 to 60	8 to 64	8 to 68
Corrected swollen joint count based on 66 joints (SJC66) at Baseline			
66 joints were assessed for swelling and joints are classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66.			
Units: units on a scale			
arithmetic mean	16.13	17.023	16.31
full range (min-max)	6 to 48	6 to 66	6 to 54

Reporting group values	GLPG0634 200 mg QD	GLPG0634 25 mg BID	GLPG0634 50 mg BID
Number of subjects	86	86	85
Age categorical			
Units: Subjects			
< 45	13	24	11
≥ 45 to < 65	58	47	59
≥ 65 to < 75	13	14	11
≥ 75	2	1	4
Age continuous			
Units: years			
arithmetic mean	54.8	52.4	55.4
full range (min-max)	19 to 75	24 to 79	21 to 78
Gender categorical			
Units: Subjects			
Female	74	68	65
Male	12	18	20
Race			
Units: Subjects			
White	67	63	65
Other	18	23	19
Black or African American	1	0	0
Asian	0	0	1
RA duration			
Units: years			
arithmetic mean	8.51	8.88	7.79
full range (min-max)	0.5 to 34.5	0.5 to 30.1	0.5 to 28.8

C-reactive protein (CRP) at Baseline			
Units: mg/L			
arithmetic mean	27.1	26.01	24.6
full range (min-max)	1 to 140.9	1.2 to 157.3	1 to 113.4
Corrected tender joint count based on 68 joints (TJC68) at Baseline			
68 joints were assessed for tenderness and joints are classified as tender/not tender giving a total possible tender joint count score of 0 to 68.			
Units: units on a scale			
arithmetic mean	28.843	25.427	27.158
full range (min-max)	8 to 68	8 to 64	8 to 66
Corrected swollen joint count based on 66 joints (SJC66) at Baseline			
66 joints were assessed for swelling and joints are classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66.			
Units: units on a scale			
arithmetic mean	17.355	15.663	17.534
full range (min-max)	6 to 58	6 to 40	6 to 62

Reporting group values	GLPG0634 100 mg BID	Total	
Number of subjects	84	594	
Age categorical			
Units: Subjects			
< 45	16	126	
≥ 45 to < 65	53	370	
≥ 65 to < 75	14	83	
≥ 75	1	15	
Age continuous			
Units: years			
arithmetic mean	53.9		
full range (min-max)	22 to 76	-	
Gender categorical			
Units: Subjects			
Female	70	481	
Male	14	113	
Race			
Units: Subjects			
White	66	443	
Other	17	146	
Black or African American	1	3	
Asian	0	2	
RA duration			
Units: years			
arithmetic mean	9.74		
full range (min-max)	0.5 to 43.2	-	
C-reactive protein (CRP) at Baseline			
Units: mg/L			
arithmetic mean	26.86		
full range (min-max)	1 to 129.4	-	
Corrected tender joint count based on 68 joints (TJC68) at Baseline			
68 joints were assessed for tenderness and joints are classified as tender/not tender giving a total possible tender joint count score of 0 to 68.			

Units: units on a scale			
arithmetic mean	25.946		
full range (min-max)	7 to 61	-	
Corrected swollen joint count based on 66 joints (SJC66) at Baseline			
66 joints were assessed for swelling and joints are classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66.			
Units: units on a scale			
arithmetic mean	16.356		
full range (min-max)	6 to 48	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo during Weeks 1 - 12; responders (having at least 20% improvement on TJC68 and SJC66) remained on placebo while nonresponders were re-randomized to 100 mg QD or 50 mg BID during Weeks 13-24	
Reporting group title	GLPG0634 50 mg QD
Reporting group description:	
GLPG0634 50 mg once daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 100 mg QD during Weeks 13-24	
Reporting group title	GLPG0634 100 mg QD
Reporting group description:	
GLPG0634 100 mg once daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 200 mg QD
Reporting group description:	
GLPG0634 200 mg once daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 25 mg BID
Reporting group description:	
GLPG0634 25 mg twice daily + placebo during Weeks 1-12; responders remained on the same treatment while non-responders switched to 50 mg BID during Weeks 13-24	
Reporting group title	GLPG0634 50 mg BID
Reporting group description:	
GLPG0634 50 mg twice daily + placebo during Weeks 1-24	
Reporting group title	GLPG0634 100 mg BID
Reporting group description:	
GLPG0634 100 mg twice daily + placebo during Weeks 1-24	
Reporting group title	Placebo Responders
Reporting group description:	
Placebo during Weeks 1 - 12; responders remained on placebo during Weeks 13-24	
Reporting group title	GLPG0634 50 mg QD Responders
Reporting group description:	
GLPG0634 50 mg once daily + placebo during Weeks 1-12; responders remained on the same treatment during Weeks 13-24	
Reporting group title	GLPG0634 25 mg BID Responders
Reporting group description:	
GLPG0634 25 mg twice daily + placebo during Weeks 1-12; responders remained on the same treatment during Weeks 13-24	
Reporting group title	Placebo Switch to GLPG0634 100 mg QD
Reporting group description:	
Some nonresponders from the placebo group were re-randomized to receive GLPG0634 100 mg once daily + placebo during Weeks 13-24	
Reporting group title	Placebo Switch to GLPG0634 50 mg BID
Reporting group description:	
Some nonresponders from the placebo group were re-randomized to receive GLPG0634 50 mg twice daily + placebo during Weeks 13-24	
Reporting group title	50 mg QD Switch to GLPG0634 100 mg QD
Reporting group description:	
Nonresponders from the 50 mg QD group were re-randomized to receive GLPG0634 100 mg once daily + placebo during Weeks 13-24	
Reporting group title	25 mg BID Switch to GLPG0634 50 mg BID

Reporting group description:

Nonresponders from the 25 mg BID group were re-randomized to receive GLPG0634 50 mg twice daily + placebo during Weeks 13-24

Reporting group title	GLPG0634 100 mg QD

Reporting group description:

GLPG0634 100 mg once daily + placebo during Weeks 1-24

Reporting group title	GLPG0634 200 mg QD

Reporting group description:

GLPG0634 200 mg once daily + placebo during Weeks 1-24

Reporting group title	GLPG0634 50 mg BID

Reporting group description:

GLPG0634 50 mg twice daily + placebo during Weeks 1-24

Reporting group title	GLPG0634 100 mg BID

Reporting group description:

GLPG0634 100 mg twice daily + placebo during Weeks 1-24

Primary: Percentage of subjects achieving an ACR20 response at Week 12

End point title	Percentage of subjects achieving an ACR20 response at Week 12

End point description:

The American College of Rheumatology (ACR) response is a measurement of improvement in multiple disease assessment criteria. The ACR20 response is defined as:
1) ≥ 20% improvement from baseline in swollen joint count based on 66 joints (SJC66), and
2) ≥ 20% improvement from baseline in tender joint count based on 68 joints (TJC68), and
3) ≥ 20% improvement from baseline in at least 3 of the following 5 items:
1. Pain visual analog scale (VAS) (taken from the Health Assessment Questionnaire – Disability Index [HAQ-DI]),
2. Patient's Global Assessment of Disease Activity VAS,
3. Physician's Global Assessment of Disease Activity VAS,
4. Total HAQ-DI score, and
5. C-reactive protein (CRP).

Intent-to-Treat (ITT) Population: all participants in the Safety Population who had post-randomization data for at least one efficacy parameter.

Non-responder imputation was used (ie, to impute a missing response, the subject was assumed to be a non-responder).

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)	44.2	56.1	63.5	68.6

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)	57	60	78.6	

Statistical analyses

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 50 mg QD
Statistical analysis description:	
Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;	
Comparison groups	Placebo v GLPG0634 50 mg QD
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1236 [1]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	26.9

Notes:

[1] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 100 mg QD
Statistical analysis description:	
Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;	
Comparison groups	Placebo v GLPG0634 100 mg QD
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0435 [2]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	19.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.7
upper limit	34

Notes:

[2] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 200 mg QD

Statistical analysis description:

Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;

Comparison groups	Placebo v GLPG0634 200 mg QD
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0068 [3]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.1
upper limit	38.8

Notes:

[3] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 25 mg BID

Statistical analysis description:

Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;

Comparison groups	Placebo v GLPG0634 25 mg BID
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1236 [4]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	27.6

Notes:

[4] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 50 mg BID

Statistical analysis description:

Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;

Comparison groups	Placebo v GLPG0634 50 mg BID
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1056 [5]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	15.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	30.6

Notes:

[5] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Statistical analysis title	ACR20 Response at Week 12 - Placebo vs 100 mg BID

Statistical analysis description:

Pairwise comparisons of each group vs. the placebo group using a logistic regression model with factors treatment group, geographical region, and prior use of biologics;

Comparison groups	Placebo v GLPG0634 100 mg BID
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [6]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	34.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.7
upper limit	48.1

Notes:

[6] - P-value has been corrected for multiplicity according to Hommel's closed-testing method.

Secondary: Percentage of subjects achieving an ACR20 response at Week 24

End point title	Percentage of subjects achieving an ACR20 response at Week 24

End point description:

ACR20 response was defined as:
1) ≥ 20% improvement from baseline in SJC66, and
2) ≥ 20% improvement from baseline in TJC68, and
3) ≥ 20% improvement from baseline in at least 3 of the following 5 items:
1. Pain VAS (taken from the HAQ-DI),
2. Patient’s Global Assessment of Disease Activity VAS,
3. Physician’s Global Assessment of Disease Activity VAS,
4. Total HAQ-DI score, and
5. CRP.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)	41.9	54.9	61.2	73.3

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)	55.8	60	79.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving an ACR50 response at Weeks 1, 2, 4, 8, 12, and 24

End point title	Percentage of subjects achieving an ACR50 response at Weeks 1, 2, 4, 8, 12, and 24

End point description:

ACR50 response was defined as:
1) ≥ 50% improvement from baseline in SJC66, and
2) ≥ 50% improvement from baseline in TJC68, and
3) ≥ 50% improvement from baseline in at least 3 of the following 5 items:
1. Pain VAS (taken from the HAQ-DI)
2. Patient’s Global Assessment of Disease Activity VAS
3. Physician’s Global Assessment of Disease Activity VAS
4. Total HAQ-DI score
5. CRP.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)				
Week 1	1.2	2.4	4.7	4.7
Week 2	5.8	7.3	20	10.5

Week 4	7	13.4	32.9	17.4
Week 8	12.8	26.8	35.3	33.7
Week 12	15.1	32.9	37.6	43
Week 24	16.3	35.4	47.1	50

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)				
Week 1	3.5	7.1	7.1	
Week 2	7	11.8	21.4	
Week 4	15.1	18.8	34.5	
Week 8	25.6	34.1	45.2	
Week 12	27.9	34.1	54.8	
Week 24	34.9	35.3	54.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving ACR70 response at Weeks 1, 2, 4, 8, 12, and 24

End point title	Percentage of subjects achieving ACR70 response at Weeks 1, 2, 4, 8, 12, and 24

End point description:

ACR70 response:
1) ≥ 70% improvement from baseline in SJC66, and
2) ≥ 70% improvement from baseline in TJC68, and
3) ≥ 70% improvement from baseline in at least 3 of the following 5 items:
1. Pain VAS (taken from the HAQ-DI),
2. Patient’s Global Assessment of Disease Activity VAS,
3. Physician’s Global Assessment of Disease Activity VAS,
4. Total HAQ-DI score, and
5. CRP.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)				
Week 1	1.2	0	0	1.2
Week 2	1.2	2.4	7.1	5.8
Week 4	3.5	7.3	14.1	4.7
Week 8	7	11	23.5	18.6
Week 12	8.1	15.9	21.2	24.4
Week 24	9.3	22	32.9	29.1

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)				
Week 1	1.2	2.4	4.8	
Week 2	2.3	5.9	3.6	
Week 4	5.8	9.4	10.7	
Week 8	9.3	14.1	27.4	
Week 12	14	18.8	31	
Week 24	20.9	23.5	39.3	

Statistical analyses

No statistical analyses for this end point

Secondary: ACR N% improvement (ACR-N) response at Weeks 1, 2, 4, 8, 12, and 24

End point title	ACR N% improvement (ACR-N) response at Weeks 1, 2, 4, 8, 12, and 24

End point description:

The ACR-N is the smallest percentage improvement in swollen and tender joints and the median of the remaining 5 core parameters, and is expected to be more sensitive to change than the ACR20, ACR50 or ACR70. It is a number varying between 0 and 100, with higher numbers indicating less severity of symptoms.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

Last observation carried forward (LOCF) algorithm was used (ie, to impute a missing value, the last preceding nonmissing value was used).

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	82	80	86
Units: units on a scale				
arithmetic mean (standard error)				
Week 1	9.27 (± 1.519)	10.31 (± 1.578)	14.69 (± 2.04)	14.25 (± 1.822)
Week 2	13.85 (± 1.949)	16.36 (± 2.125)	25.2 (± 2.986)	22.61 (± 2.517)
Week 4	16.93 (± 2.332)	21.08 (± 2.598)	31.32 (± 3.354)	27.45 (± 2.573)
Week 8	21.6 (± 2.644)	30.16 (± 3.015)	38.24 (± 3.484)	37.88 (± 3.097)
Week 12	23.09 (± 2.911)	34.03 (± 3.335)	39.87 (± 3.449)	42.1 (± 3.277)
Week 24	22.06 (± 2.846)	37.13 (± 3.582)	50.86 (± 3.645)	50.4 (± 3.291)

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	85	82	
Units: units on a scale				
arithmetic mean (standard error)				
Week 1	9.01 (± 1.603)	11.36 (± 1.939)	17.63 (± 2.206)	
Week 2	15.2 (± 2.063)	20.01 (± 2.47)	27.77 (± 2.606)	
Week 4	23.17 (± 2.668)	26.37 (± 2.961)	35.69 (± 2.861)	
Week 8	31.2 (± 2.845)	33.4 (± 3.15)	45.36 (± 3.246)	
Week 12	34.12 (± 3.144)	35.86 (± 3.29)	51.17 (± 3.379)	
Week 24	38.56 (± 3.384)	40.5 (± 3.299)	58.69 (± 3.204)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with Disease Activity Score 28 Joints Corrected for CRP (DAS28 (CRP)) European League Against Rheumatism (EULAR) response at Weeks 1, 2, 4, 8, 12, and 24

End point title	Percentage of subjects with Disease Activity Score 28 Joints Corrected for CRP (DAS28 (CRP)) European League Against Rheumatism (EULAR) response at Weeks 1, 2, 4, 8, 12, and 24

End point description:

DAS28 (CRP) was categorized into EULAR response categories (none, moderate, good) as follows:
None = Actual DAS28 (CRP) ≤ 3.2, > 3.2 to ≤ 5.1, or > 5.1 AND Improvement in DAS28 (CRP) from baseline ≤ 6.0 or > 0.6 to ≤ 1.2;
Moderate = Actual DAS28 (CRP) ≤ 3.2 AND Improvement in DAS28 (CRP) from baseline > 0.6 to ≤ 1.2, Actual DAS28 (CRP) > 3.2 to ≤ 5.1 or > 5.1 AND Improvement in DAS28 (CRP) from baseline > 1.2, or Actual DAS28 (CRP) > 3.2 to ≤ 5.1 AND Improvement in DAS28 (CRP) from baseline > 0.6 to ≤ 1.2;
Good = Actual DAS28 (CRP) ≤ 3.2 AND Improvement in DAS28 (CRP) from baseline > 1.2.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

LOCF algorithm was used.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)				
Week 1: None	73	61	58	42
Week 1: Moderate	21	38	35	55
Week 1: Good	6	1	7	3
Week 2: None	58	49	39	31
Week 2: Moderate	33	45	42	53
Week 2: Good	9	6	19	15
Week 4: None	56	44	29	16
Week 4: Moderate	34	46	40	65
Week 4: Good	10	10	31	19
Week 8: None	44	34	20	15
Week 8: Moderate	43	45	52	49
Week 8: Good	13	21	28	36
Week 12: None	41	33	18	8
Week 12: Moderate	45	44	48	55
Week 12: Good	14	23	34	37
Week 24: None	48	33	12	10
Week 24: Moderate	34	35	38	38
Week 24: Good	19	32	51	51

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)				
Week 1: None	63	64	40	

Week 1: Moderate	34	32	49	
Week 1: Good	3	5	11	
Week 2: None	51	44	20	
Week 2: Moderate	43	46	62	
Week 2: Good	6	11	18	
Week 4: None	37	35	15	
Week 4: Moderate	44	42	61	
Week 4: Good	19	22	24	
Week 8: None	24	24	8	
Week 8: Moderate	51	49	46	
Week 8: Good	24	27	45	
Week 12: None	28	15	7	
Week 12: Moderate	44	56	43	
Week 12: Good	28	28	50	
Week 24: None	23	14	5	
Week 24: Moderate	37	49	31	
Week 24: Good	40	36	64	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving ACR/EULAR remission at Weeks 2, 4, 8, 12, and 24

End point title	Percentage of subjects achieving ACR/EULAR remission at Weeks 2, 4, 8, 12, and 24

End point description:

A subject's disease activity status can be defined as being in remission when scores on the TJC28, SJC28, CRP (actual value in mg/dL) and Patient Global Assessment of Disease Activity (cm) are all ≤ 1.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

Non-responder imputation was used.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: percentage of subjects				
number (not applicable)				
Week 2	0	0	3.5	0
Week 4	1.2	1.2	1.2	2.3
Week 8	1.2	3.7	3.5	3.5
Week 12	3.5	3.7	3.5	5.8
Week 24	1.2	11	8.2	11.6

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84	
Units: percentage of subjects				
number (not applicable)				
Week 2	0	0	1.2	
Week 4	0	0	2.4	
Week 8	1.2	1.2	3.6	
Week 12	4.7	4.7	9.5	
Week 24	5.8	3.5	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Simplified Disease Activity Index (SDAI) at baseline and change from baseline at Weeks 1, 2, 4, 8, 12, and 24

End point title	Simplified Disease Activity Index (SDAI) at baseline and change from baseline at Weeks 1, 2, 4, 8, 12, and 24

End point description:

The SDAI is the numerical sum of 5 outcome parameters: TJC28, SJC28, Patient Global Assessment of Disease Activity (in cm), Physician's Global Assessment of Disease Activity (in cm), and CRP (mg/dL).

The SDAI was categorized as follows:
• High disease activity: SDAI > 26
• Moderate disease activity: 11 to 26
• Low disease activity: 3.3 to 11
• Remission: ≤ 3.3.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

LOCF algorithm was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	43.756 (± 1.2717)	43.77 (± 1.3499)	45.42 (± 1.3909)	45.611 (± 1.3362)
Change at Week 1	-8.3 (± 1.25)	-8 (± 1.14)	-12.2 (± 1.45)	-12.8 (± 1.29)

Change at Week 2	-11.4 (± 1.45)	-12.5 (± 1.46)	-18.6 (± 1.64)	-16.4 (± 1.35)
Change at Week 4	-13.1 (± 1.47)	-16.3 (± 1.64)	-22.7 (± 1.78)	-22.2 (± 1.28)
Change at Week 8	-16.3 (± 1.64)	-20.1 (± 1.86)	-24.6 (± 1.57)	-25.9 (± 1.57)
Change at Week 12	-16.3 (± 1.84)	-21 (± 1.84)	-25.2 (± 1.69)	-27.2 (± 1.55)
Change at Week 24	-15.8 (± 2)	-22.8 (± 2.07)	-30.1 (± 1.66)	-31 (± 1.62)

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86[7]	85	84	
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	43.951 (± 1.3224)	44.794 (± 1.4043)	44.542 (± 1.3097)	
Change at Week 1	-8.2 (± 1.17)	-10 (± 1.22)	-14.5 (± 1.31)	
Change at Week 2	-13.4 (± 1.29)	-15.1 (± 1.43)	-20.3 (± 1.35)	
Change at Week 4	-17.8 (± 1.44)	-19.3 (± 1.74)	-24.9 (± 1.54)	
Change at Week 8	-22.2 (± 1.68)	-23.2 (± 1.8)	-29.2 (± 1.58)	
Change at Week 12	-22.3 (± 1.71)	-24.5 (± 1.87)	-30.6 (± 1.57)	
Change at Week 24	-24.9 (± 1.85)	-27.9 (± 2)	-34.4 (± 1.47)	

Notes:

[7] - Except for at Baseline (N = 85)

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Disease Activity Index (CDAI) at baseline and change from baseline at Weeks 1, 2, 4, 8, 12, and 24

End point title	Clinical Disease Activity Index (CDAI) at baseline and change from baseline at Weeks 1, 2, 4, 8, 12, and 24

End point description:

The CDAI is the SDAI modified to exclude CRP and is the sum of the 4 outcome parameters: TJC28, SJC28, Patient Global Assessment of Disease Activity (in cm), and Physician’s Global Assessment of Disease Activity (in cm).

The CDAI was be categorized as follows:
• High disease activity: > 22
• Moderate disease activity: 10 to 22
• Mild disease activity: 2.8 to 10
• Remission: ≤ 2.8.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

LOCF algorithm was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85	86
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	42.131 (± 1.236)	40.999 (± 1.2104)	42.966 (± 1.3014)	42.901 (± 1.2844)
Change at Week 1	-8.5 (± 1.23)	-7.2 (± 1.09)	-11.1 (± 1.38)	-11.1 (± 1.22)
Change at Week 2	-11.6 (± 1.43)	-11.7 (± 1.39)	-17.3 (± 1.58)	-14.6 (± 1.29)
Change at Week 4	-13.3 (± 1.42)	-15.2 (± 1.54)	-21.4 (± 1.71)	-20.4 (± 1.24)
Change at Week 8	-16.4 (± 1.58)	-18.9 (± 1.78)	-23.4 (± 1.52)	-24.2 (± 1.5)
Change at Week 12	-16.6 (± 1.84)	-19.7 (± 1.77)	-23.8 (± 1.66)	-25.5 (± 1.5)
Change at Week 24	-16 (± 1.95)	-21.3 (± 1.97)	-28.6 (± 1.63)	-29.4 (± 1.5)

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86[8]	85	84	
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	41.347 (± 1.2442)	42.333 (± 1.3186)	41.856 (± 1.2462)	
Change at Week 1	-7.3 (± 1.14)	-9 (± 1.15)	-12.8 (± 1.27)	
Change at Week 2	-12.4 (± 1.26)	-14 (± 1.38)	-18.4 (± 1.31)	
Change at Week 4	-17.1 (± 1.35)	-18 (± 1.71)	-22.8 (± 1.51)	
Change at Week 8	-21.1 (± 1.67)	-21.9 (± 1.75)	-27.1 (± 1.53)	
Change at Week 12	-21.3 (± 1.65)	-23.2 (± 1.81)	-28.5 (± 1.49)	
Change at Week 24	-23.8 (± 1.75)	-26.7 (± 1.9)	-32.4 (± 1.39)	

Notes:

[8] - Except for Baseline (N = 85)

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life using the functional assessment of chronic illness therapy [FACIT] Fatigue Score at baseline and change from baseline at Weeks 4, 12, and 24

End point title	Quality of Life using the functional assessment of chronic illness therapy [FACIT] Fatigue Score at baseline and change from baseline at Weeks 4, 12, and 24

End point description:

FACIT-Fatigue scale is a 13-item questionnaire, each scored on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the subject's response to the questions (with the exception of 2 negatively stated that are scored reversely), the greater the fatigue. The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score), with a higher score indicating a better quality of life.

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

LOCF algorithm was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85[9]	86
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	26.2 (± 1.09)	26.2 (± 1.1)	26.6 (± 1.06)	25.2 (± 1.25)
Change at Week 4	4.9 (± 1.06)	4.4 (± 1.11)	9.1 (± 1.14)	8.5 (± 1.23)
Change at Week 12	5.6 (± 1.06)	7.6 (± 1.26)	9.5 (± 1.21)	11.4 (± 1.37)
Change at Week 24	6 (± 1.04)	7.9 (± 1.21)	11.1 (± 1.2)	11.6 (± 1.33)

Notes:

[9] - Except at Baseline (N = 84)

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84[10]	
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	28.1 (± 1.18)	26.2 (± 1.04)	25.6 (± 1.25)	
Change at Week 4	4.5 (± 1.06)	6.6 (± 0.88)	9.9 (± 0.97)	
Change at Week 12	6.9 (± 1.12)	8.4 (± 1.08)	11.3 (± 1.25)	
Change at Week 24	7.7 (± 1.17)	9 (± 1.04)	12.8 (± 1.36)	

Notes:

[10] - Except at Baseline (N = 83)

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life using the Short Form-36 (SF-36) scores at baseline and change from baseline at Weeks 4, 12, and 24

End point title	Quality of Life using the Short Form-36 (SF-36) scores at baseline and change from baseline at Weeks 4, 12, and 24

End point description:

The SF-36 is a 36-item questionnaire measuring 8 domains (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health). Each domain score ranges from 0 (worst) to 100 (best), with higher scores reflecting better health-related functional status. Two summary scale scores were computed based on weighted combinations of the 8 domain scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS).

Intent-to-Treat (ITT) Population. Subjects who switched treatment at Week 12 were handled as if they discontinued at Week 12.

LOCF algorithm was used.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 12, and 24

End point values	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	82	85[11]	86
Units: units on a scale				
arithmetic mean (standard error)				
PCS at Baseline	32.999 (± 0.7121)	32.691 (± 0.7474)	31.636 (± 0.7926)	31.625 (± 0.6355)
PSC Change at Week 4	3 (± 0.65)	4.1 (± 0.88)	6.1 (± 0.98)	6.4 (± 0.87)
PSC Change at Week 12	3.2 (± 0.74)	6.7 (± 1)	8.4 (± 0.93)	8.9 (± 0.9)
PSC Change at Week 24	2.8 (± 0.75)	7.3 (± 1.02)	9.9 (± 1.09)	9.7 (± 0.99)
MCS at Baseline	42.849 (± 1.0861)	42.199 (± 1.2581)	43.953 (± 1.1118)	41.362 (± 1.1427)
MCS Change at Week 4	3 (± 0.92)	3.4 (± 0.91)	4.9 (± 0.85)	5.4 (± 0.98)
MCS Change at Week 12	4.3 (± 1.05)	4.4 (± 1.11)	5.1 (± 0.96)	8.1 (± 1.17)
MCS Change at Week 24	4.7 (± 0.96)	4.3 (± 1.04)	6.7 (± 0.91)	7.2 (± 1.12)

Notes:

[11] - Except at Baseline (N = 84)

End point values	GLPG0634 25 mg BID	GLPG0634 50 mg BID	GLPG0634 100 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	85	84[12]	
Units: units on a scale				
arithmetic mean (standard error)				
PCS at Baseline	31.634 (± 0.6858)	31.332 (± 0.726)	32.249 (± 0.7844)	
PSC Change at Week 4	5 (± 0.69)	4.2 (± 0.8)	7.2 (± 0.77)	
PSC Change at Week 12	7.5 (± 0.92)	7.1 (± 0.96)	10.5 (± 0.98)	
PSC Change at Week 24	7.8 (± 0.85)	7.9 (± 0.91)	11.6 (± 1.1)	
MCS at Baseline	45.527 (± 1.288)	44.748 (± 1.228)	42.059 (± 1.2898)	
MCS Change at Week 4	2.4 (± 0.78)	2.7 (± 0.84)	5.6 (± 0.92)	
MCS Change at Week 12	3.5 (± 0.97)	3.1 (± 1.02)	6.2 (± 0.98)	
MCS Change at Week 24	3.8 (± 0.96)	3.5 (± 1.01)	7.1 (± 1.21)	

Notes:

[12] - Except at Baseline (N = 83)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through end of study drug treatment (average exposure: 160.7 days) plus 10 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the Placebo group during Weeks 1-12.

Subjects who switched treatment at Week 12 were included in the other groups of the same dose for adverse events reported during Weeks 13-24.

Reporting group title	GLPG0634 50 mg QD

Reporting group description:

Adverse events reported in this group include all subjects randomized to the GLPG0634 50 mg QD group during Weeks 1-12 and responders in this group during Weeks 13-24.

Subjects who switched treatment at Week 12 were included in the other groups of the same dose for adverse events reported during Weeks 13-24.

Reporting group title	GLPG0634 100 mg QD

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the GLPG0634 100 mg QD group during Weeks 1-24, some nonresponders originally randomized to the Placebo group during Weeks 13-24, and all nonresponders originally randomized to the GLPG0634 50 mg QD group during Weeks 13-24.

Subjects who switched treatment at Week 12 were included in the other groups of the same dose for adverse events reported during Weeks 13-24.

Reporting group title	GLPG0634 200 mg QD

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the GLPG0634 200 mg QD group during Weeks 1-24.

Reporting group title	GLPG0634 25 mg BID

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the GLPG0634 25 mg BID group during Weeks 1-12 and responders in this group during Weeks 13-24.

Subjects who switched treatment at Week 12 were included in the other groups of the same dose for adverse events reported during Weeks 13-24.

Reporting group title	GLPG0634 50 mg BID

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the GLPG0634 50 mg BID group during Weeks 1-24, some nonresponders originally randomized to the Placebo group during Weeks 13-24, and all nonresponders originally randomized to the GLPG0634 25 mg BID group during Weeks 13-24.

Subjects who switched treatment at Week 12 were included in the other groups of the same dose for adverse events reported during Weeks 13-24.

Reporting group title	GLPG0634 100 mg BID

Reporting group description:

Adverse events reported in this group includes all subjects randomized to the GLPG0634 100 mg BID group during Weeks 1-24.

Serious adverse events	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 86 (4.65%)	0 / 82 (0.00%)	4 / 119 (3.36%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (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
Angina unstable			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
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 myocardial infarction			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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 complete			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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			
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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			
Inflammation			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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			
Vertigo			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (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			
Muscle twitching			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (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

Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (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
Pneumonia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic gangrene			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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 discitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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 / 86 (0.00%)	0 / 82 (0.00%)	0 / 119 (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			
Dehydration			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (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

Serious adverse events	GLPG0634 200 mg QD	GLPG0634 25 mg BID	GLPG0634 50 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 86 (2.33%)	2 / 86 (2.33%)	0 / 117 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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			
Abortion spontaneous			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	0 / 117 (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
Abortion spontaneous complete			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	0 / 117 (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
Nervous system disorders			

Ischaemic cerebral infarction			
subjects affected / exposed	0 / 86 (0.00%)	1 / 86 (1.16%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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
Pancytopenia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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			
Vertigo			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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			
Muscle twitching			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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			

Appendicitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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
Diabetic gangrene			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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
Erysipelas			
subjects affected / exposed	1 / 86 (1.16%)	0 / 86 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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			
Dehydration			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	0 / 117 (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	GLPG0634 100 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 84 (3.57%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous complete			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic cerebral infarction			

subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Appendicitis			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Diabetic gangrene			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 84 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	GLPG0634 50 mg QD	GLPG0634 100 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 86 (51.16%)	39 / 82 (47.56%)	48 / 119 (40.34%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 86 (2.33%)	3 / 82 (3.66%)	6 / 119 (5.04%)
occurrences (all)	2	3	6
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 86 (4.65%)	1 / 82 (1.22%)	1 / 119 (0.84%)
occurrences (all)	4	5	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 86 (3.49%)	7 / 82 (8.54%)	0 / 119 (0.00%)
occurrences (all)	3	8	0
Vomiting			
subjects affected / exposed	1 / 86 (1.16%)	0 / 82 (0.00%)	0 / 119 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 82 (1.22%)	1 / 119 (0.84%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	4 / 86 (4.65%)	8 / 82 (9.76%)	3 / 119 (2.52%)
occurrences (all)	4	8	3
Upper respiratory tract infection			
subjects affected / exposed	1 / 86 (1.16%)	2 / 82 (2.44%)	2 / 119 (1.68%)
occurrences (all)	1	2	2
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 86 (0.00%)	2 / 82 (2.44%)	0 / 119 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	GLPG0634 200 mg QD	GLPG0634 25 mg BID	GLPG0634 50 mg BID
Total subjects affected by non-serious adverse events			

subjects affected / exposed	50 / 86 (58.14%)	44 / 86 (51.16%)	57 / 117 (48.72%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 86 (4.65%)	3 / 86 (3.49%)	4 / 117 (3.42%)
occurrences (all)	4	3	4
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 86 (6.98%)	6 / 86 (6.98%)	3 / 117 (2.56%)
occurrences (all)	8	6	6
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 86 (3.49%)	3 / 86 (3.49%)	3 / 117 (2.56%)
occurrences (all)	3	4	4
Vomiting			
subjects affected / exposed	0 / 86 (0.00%)	0 / 86 (0.00%)	6 / 117 (5.13%)
occurrences (all)	0	0	7
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 86 (2.33%)	5 / 86 (5.81%)	2 / 117 (1.71%)
occurrences (all)	4	5	2
Nasopharyngitis			
subjects affected / exposed	3 / 86 (3.49%)	4 / 86 (4.65%)	2 / 117 (1.71%)
occurrences (all)	3	4	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 86 (4.65%)	4 / 86 (4.65%)	6 / 117 (5.13%)
occurrences (all)	5	4	7
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	5 / 86 (5.81%)	2 / 86 (2.33%)	1 / 117 (0.85%)
occurrences (all)	5	2	1

Non-serious adverse events	GLPG0634 100 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 84 (53.57%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 2 / 84 (2.38%) 4		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 84 (1.19%) 1 2 / 84 (2.38%) 3		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 84 (1.19%) 1 4 / 84 (4.76%) 6 2 / 84 (2.38%) 2		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	 4 / 84 (4.76%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2013	• Due to the implementation of a new method for CRP measurements carried out by the central laboratory (Quest Diagnostics), the ULN and its fold change that were used to calculate the numeric value for the inclusion criteria were likely to change. Therefore, instead of a numeric value, CRP as inclusion criterion was expressed as a 1.5-fold change ULN. • As adjustments for the body surface area were not going to be carried out (Cockroft-Gault formula), the estimated creatinine clearance was expressed as mL/min. • In order to reduce the recording burden for subjects included in the study, the date and time of the taken capsules was recorded on selected visits only and not at every visit. • To confirm the absence of interaction of GLPG0634 on MTX disposition in a broader population of subjects with RA, the measurement of MTX and its metabolite (7-hydroxy-methotrexate) in plasma samples collected in the study could be performed. • Size of the SST tubes that were planned to be used for the additional PD assessment, was changed (instead of two 4-mL SST tubes, only one 8.5-mL SST tube was collected). • Due to the administration of MTX in this study, the expectedness of AEs arising due to the use of MTX was determined in the definitions for unexpected adverse events/safety information.
17 April 2013	Introduced stratification according to the previous use of a biological DMARD in a single clinical study setting, in addition to the stratification according to region. This aimed to obtain equal distribution of subjects, who had been previously exposed to a biological DMARD during a single clinical study setting between the study groups, to reduce heterogeneity and therefore be beneficial for results interpretation. Consequently the statistical methods section was adapted accordingly: Cochran-Mantel-Haenszel and logrank tests, both controlling for region, were changed to logistic and proportional hazards regression models in order to include more factors.
02 August 2013	This amendment was applicable for all countries apart from France and the US and addressed specific comments received from Competent Authorities and Ethics Committees. • The overall benefit/risk assessment was updated in view of recent advances in the product development and the current status of the scientific field for JAK development. • The inclusion/exclusion criteria were refined with further specified and strengthened laboratory test limits, and additional criteria to manage the overall health status at Screening were introduced. • Criteria for individual subject withdrawal were further specified. • An independent DSMB was introduced. • The section on prior and concomitant therapy was updated.
20 May 2014	This amendment was applicable for all countries apart from France and the US. • The inclusion/exclusion criteria were adjusted to better represent the current RA population without compromising the study objective, including a decrease in entry level for CRP to > 0.70 x ULN. • The individual subject withdrawal criteria were adjusted. • The general study procedures (calendar days, re-Screening and retesting guidelines) were refined to provide further guidance to investigators. • In addition, the protocol amendment included an update of the background information on GLPG0634 and the benefit/risk section in accordance with the current version of the IB (Edition 7.0, February 2014).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported