Clinical trial results:
Double-Blind, Randomized, Placebo-Controlled, Multi Centre Study to Investigate the Efficacy and Safety of GLPG0634 in Subjects With Active Crohn's Disease With Evidence of Mucosal Ulceration

Summary

EudraCT number	2013-002857-32
Trial protocol	DE HU CZ GB BE PL
Global end of trial date	30 December 2015

Results information

Result version number	v1 (current)
This version publication date	06 January 2017
First version publication date	06 January 2017

Trial information

Trial identification

Sponsor protocol code	GLPG0634-CL-211

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02048618
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Clinical Trial Information Desk, Galapagos NV, +32 15342 900, rd@glpg.com
Scientific contact	Clinical Trial Information Desk, Galapagos NV, +32 15342 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	30 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate efficacy in terms of the percentage of subjects achieving clinical remission (CD Activity Index [CDAI] score < 150) following 10 weeks treatment with GLPG0634 200 mg q.d. versus placebo in patients with active CD with evidence of mucosal ulceration.

Protection of trial subjects:

Before implementing this study, the protocol, the proposed informed consent, and other information to subjects was to be reviewed by an Independent Ethics Committee (IEC). A signed and dated statement that the protocol and informed consent was approved by the IEC had to be given to the CRO before study initiation. The IEC, as required by local law, had to approve any amendments to the protocol, which needed formal approval. The IEC could be notified for all other amendments (i.e. administrative changes in accordance with local requirements).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2014
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: 32
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Romania: 11
Worldwide total number of subjects	174
EEA total number of subjects	152

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)	169
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe. The first participant was screened on 3 February 2014. The last study visit occurred on 30 December 2015.

Pre-assignment

Screening details:

311 subjects were screened.

Period 1

Period 1 title	Period 1: Weeks 1 - 10
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 - 10; responders (having at least reduction in CDAI of 100 points) remained on placebo while nonresponders were re-randomized to GLPG0634 100 mg QD during Weeks 11 - 20.

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

Dosage and administration details:

2 placebo tablets in the morning.

Arm title	GLPG0634 200 mg QD

Arm description:

GLPG0634 200 mg once daily during Weeks 1 - 10; responders (having at least reduction in CDAI of 100 points) were re-randomized to GLPG0634 200 mg QD, GLPG0634 100 mg QD, or placebo during Weeks 11 - 20; nonresponders were re-randomized to GLPG0634 200 mg QD or placebo during Weeks 11 - 20.

Arm type	Experimental
Investigational medicinal product name	GLPG0634 200 mg QD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 GLPG0634 tablets in the morning.

Number of subjects in period 1	Placebo	GLPG0634 200 mg QD
Started	44	130
Completed	37	111
Not completed	7	19
Consent withdrawn by subject	1	3
Treatment failure	3	10
Adverse event, non-fatal	3	4
Other	-	1
Lost to follow-up	-	1

Period 2	
Period 2 title	Period 2: Weeks 11 - 20
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 -10; responders remained on placebo during Weeks 11 -20.

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

Dosage and administration details:

2 placebo tablets in the morning.

Arm title	Placebo nonresponders

Arm description:

Placebo during Weeks 1 - 10; nonresponders were re-randomized to received GLPG0634 100 mg QD + placebo during Weeks 11 - 20.

Arm type	Experimental
Investigational medicinal product name	GLPG0634 100 mg QD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 GLPG0634 100 mg tablet + placebo once daily in the morning.

Arm title	GLPG0634 200 mg QD to GLPG0634 200 mg QD

Arm description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders and some nonresponders were re-randomized to GLPG0634 200 mg QD during Weeks 11 - 20.	
Arm type	Experimental
Investigational medicinal product name	GLPG0634 200 mg QD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
2 GLPG0634 tablets in the morning.	
Arm title	GLPG0634 200 mg QD switch to GLPG0634 100 mg QD
Arm description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders were re-randomized to GLPG0634 100 mg QD during Weeks 11 - 20.	
Arm type	Experimental
Investigational medicinal product name	GLPG0634 100 mg QD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
1 GLPG0634 100 mg tablet + placebo once daily in the morning.	
Arm title	GLPG0634 200 mg QD switch to placebo
Arm description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders and some nonresponders were re-randomized to placebo during Weeks 11 - 20.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
2 placebo tablets in the morning.	

Number of subjects in period 2[1]	Placebo Responders	Placebo nonresponders	GLPG0634 200 mg QD to GLPG0634 200 mg QD
Started	15	22	57
Completed	12	20	45
Not completed	3	2	12
Consent withdrawn by subject	1	-	3
Treatment failure	1	2	6
Adverse event, non-fatal	1	-	3

Number of subjects in period 2[1]	GLPG0634 200 mg QD switch to GLPG0634 100 mg	GLPG0634 200 mg QD switch to placebo

	QD	
Started	30	23
Completed	25	21
Not completed	5	2
Consent withdrawn by subject	1	2
Treatment failure	2	-
Adverse event, non-fatal	2	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject in the GLPG0634 200 mg QD treatment group completed study part 1, was re-randomized into the same group, but was not exposed during study part 2, resulting in 57 subjects in the continued GLPG0634 200 mg QD treatment group.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo during Weeks 1 - 10; responders (having at least reduction in CDAI of 100 points) remained on placebo while nonresponders were re-randomized to GLPG0634 100 mg QD during Weeks 11 - 20.	
Reporting group title	GLPG0634 200 mg QD
Reporting group description:	
GLPG0634 200 mg once daily during Weeks 1 - 10; responders (having at least reduction in CDAI of 100 points) were re-randomized to GLPG0634 200 mg QD, GLPG0634 100 mg QD, or placebo during Weeks 11 - 20; nonresponders were re-randomized to GLPG0634 200 mg QD or placebo during Weeks 11 - 20.	

Reporting group values	Placebo	GLPG0634 200 mg QD	Total
Number of subjects	44	130	174
Age categorical Units: Subjects			
Adults (18-64 years)	43	126	169
From 65-84 years	1	4	5
Age continuous Units: years			
arithmetic mean	35.1	37.4	
full range (min-max)	18 to 71	18 to 68	-
Gender categorical Units: Subjects			
Female	26	71	97
Male	18	59	77
Race Units: Subjects			
White	43	117	160
Other	1	13	14
BMI Units: kg/m²			
arithmetic mean	23.87	23.78	
full range (min-max)	18.1 to 40.4	14.8 to 37	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo during Weeks 1 - 10; responders (having at least reduction in CDAI of 100 points) remained on placebo while nonresponders were re-randomized to GLPG0634 100 mg QD during Weeks 11 - 20.	
Reporting group title	GLPG0634 200 mg QD
Reporting group description:	
GLPG0634 200 mg once daily during Weeks 1 - 10; responders (having at least reduction in CDAI of 100 points) were re-randomized to GLPG0634 200 mg QD, GLPG0634 100 mg QD, or placebo during Weeks 11 - 20; nonresponders were re-randomized to GLPG0634 200 mg QD or placebo during Weeks 11 - 20.	
Reporting group title	Placebo Responders
Reporting group description:	
Placebo during Weeks 1 -10; responders remained on placebo during Weeks 11 -20.	
Reporting group title	Placebo nonresponders
Reporting group description:	
Placebo during Weeks 1 - 10; nonresponders were re-randomized to received GLPG0634 100 mg QD + placebo during Weeks 11 - 20.	
Reporting group title	GLPG0634 200 mg QD to GLPG0634 200 mg QD
Reporting group description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders and some nonresponders were re-randomized to GLPG0634 200 mg QD during Weeks 11 - 20.	
Reporting group title	GLPG0634 200 mg QD switch to GLPG0634 100 mg QD
Reporting group description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders were re-randomized to GLPG0634 100 mg QD during Weeks 11 - 20.	
Reporting group title	GLPG0634 200 mg QD switch to placebo
Reporting group description:	
GLPG0634 200 mg QD during Weeks 1 - 10; some responders and some nonresponders were re-randomized to placebo during Weeks 11 - 20.	

Primary: Clinical remission (CDAI) at Week 10

End point title	Clinical remission (CDAI) at Week 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

CDAI clinical remission is defined as a CDAI score of < 150.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline 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 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: percentage of subjects				
number (not applicable)	22.7	46.9		

Statistical analyses

Statistical analysis title	CDAI Clinical Remission at Week 10
Comparison groups	Placebo v GLPG0634 200 mg QD
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0077 [1]
Method	Regression, Logistic
Parameter estimate	Difference in percentage rates
Point estimate	24.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	9
upper limit	39.2

Notes:

[1] - type III p-value from a logistic regression model per time point, with factors: treatment, baseline use of oral GCSs
(yes/no), screening CRP (≤ 10 mg/L/> 10 mg/L), and previous use of anti-TNFs (naïve/experienced).

Secondary: Clinical remission (CDAI) at Weeks 2, 4, and 6

End point title	Clinical remission (CDAI) at Weeks 2, 4, and 6

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

CDAI clinical remission is defined as a CDAI score of < 150.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline 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	Secondary
End point timeframe:	
Weeks 2, 4, and 6	

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: percentage of subjects				
number (not applicable)				
Week 2	20.5	21.9		
Week 4	18.2	33.6		
Week 6	27.3	40.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response (CDAI) at Weeks 2, 4, 6, and 10

End point title	Clinical response (CDAI) at Weeks 2, 4, 6, and 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

CDAI clinical response is defined as a change from baseline in CDAI score of <= -100 points.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline 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	Secondary
End point timeframe:	
Weeks 2, 4, 6, and 10	

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: percentage of subjects				
number (not applicable)				
Week 2	29.5	37.5		
Week 4	31.8	40.6		
Week 6	50	58.6		
Week 10	40.9	59.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Endoscopic response, endoscopic remission, and mucocal healing (SES-CD) at Week 10

End point title	Endoscopic response, endoscopic remission, and mucocal healing (SES-CD) at Week 10

End point description:

The simplified endoscopic activity score for Crohn's disease (SES-CD) is an endoscopy-based scoring system assessing the ileum, right colon, transverse colon, left colon, and rectum bowel segments for the presence of ulcers, the percentage of ulcerated surface, the percentage of affected surface, and the presence of narrowing.

Endoscopic 50% response is defined as a change from baseline in SES-CD score <= -50.
Endoscopic 25% response is defined as a change from baseline in SES-CD score <= -25.
Endoscopic remission is defined as a SES-CD score <= 4, with ulcerated surface subscore <= 1 in all 5 segments.
Mucosal healing is defined as a SES-CD score of 0.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline 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	Secondary

End point timeframe:

Week 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: percentage of subjects				
number (not applicable)				
Endoscopic 50% response	18.2	25		
Endoscopic 25% response	36.4	37.5		
Endoscopic remission	6.8	13.3		
Mucosal healing	2.3	2.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CDAI score at Weeks 2, 4, 6, and 10

End point title	Change from baseline in CDAI score at Weeks 2, 4, 6, and 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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 2, 4, 6, and 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)				
Week 2	-70 (± 12.03)	-74.4 (± 6.61)		
Week 4	-66.1 (± 14.08)	-91.2 (± 6.98)		
Week 6	-83.7 (± 14.6)	-110.6 (± 7.27)		
Week 10	-94.1 (± 16.58)	-127.7 (± 8.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in SES-CD score at Week 10

End point title	Change from baseline in SES-CD score at Week 10

End point description:

The simplified endoscopic activity score for Crohn's disease (SES-CD) is an endoscopy-based scoring system assessing the ileum, right colon, transverse colon, left colon, and rectum bowel segments for the presence of ulcers, the percentage of ulcerated surface, the percentage of affected surface, and the presence of narrowing.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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:

Week 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)	-2.7 (± 0.93)	-2.6 (± 0.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in D'Haens histopathology score at Week 10

End point title	Change from baseline in D'Haens histopathology score at Week 10

End point description:

The D'Haens score is a histpathological scoring system for Crohn's disease. The scoring system contains 8 histological variables that are scored independently, with grading from 0-3. The total score is the sum of all individual scores(min=0, max=16).

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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:

Week 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)	-0.6 (± 1.91)	-3.5 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in IBDQ score at Week 10

End point title	Change from baseline in IBDQ score at Week 10

End point description:

The inflammatory bowel disease questionnaire (IBDQ) is a 32-item disease-specific quality-of-life questionnaire consisting of 4 domains (bowel symptoms, emotional function, social function, and systemic symptoms), which was designed to evaluate the effects of drug therapy in patients with IBD.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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:

Week 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from basleline				
arithmetic mean (standard error)	17.56 (± 5.085)	33.82 (± 2.978)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CDAI pain subscore at Weeks 2, 4, 6, and 10

End point title	Change from baseline in CDAI pain subscore at Weeks 2, 4, 6, and 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being

4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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 2, 4, 6, and 10	

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)				
Week 2	-0.57 (± 0.094)	-0.53 (± 0.058)		
Week 4	-0.5 (± 0.105)	-0.63 (± 0.058)		
Week 6	-0.6 (± 0.106)	-0.76 (± 0.064)		
Week 10	-0.65 (± 0.119)	-0.86 (± 0.068)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CDAI liquid stools subscore at Weeks 2, 4, 6, and 10

End point title	Change from baseline in CDAI liquid stools subscore at Weeks 2, 4, 6, and 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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 2, 4, 6, and 10	

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)				
Week 2	-1.1 (± 0.271)	-1.29 (± 0.148)		
Week 4	-1.17 (± 0.265)	-1.54 (± 0.175)		
Week 6	-1.42 (± 0.303)	-2.03 (± 0.192)		
Week 10	-1.57 (± 0.367)	-2.26 (± 0.214)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CDAI general well-being subscore at Weeks 2, 4, 6, and 10

End point title	Change from baseline in CDAI general well-being subscore at Weeks 2, 4, 6, and 10

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

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 2, 4, 6, and 10	

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: change from baseline				
arithmetic mean (standard error)				
Week 2	-0.47 (± 0.111)	-0.6 (± 0.071)		
Week 4	-0.45 (± 0.135)	-0.7 (± 0.068)		
Week 6	-0.64 (± 0.14)	-0.83 (± 0.072)		
Week 10	-0.65 (± 0.132)	-0.98 (± 0.076)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to CDAI clinical remission

End point title	Time to CDAI clinical remission

End point description:

The Crohn's Disease Activity Index (CDAI) is a measurement of disease activity using multiple disease assessment criteria. The CDAI is a composite scoring index based on the following categories:
1) Number of liquid or very soft stools
2) Abdominal pain
3) General well being
4) Extra-intestinal manifestations of Crohn’s Disease
5) Lomotil/ Imodium/opiates for diarrhea
6) Abdominal mass
7) Hematocrit (%)
8) Body Weight

CDAI clinical remission is defined as a CDAI score of < 150.

Intent-to-Treat (ITT) Population: all subjects randomized, exposed at least once, and with post-Baseline data for at least one efficacy parameter.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, and 10

End point values	Placebo	GLPG0634 200 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	128		
Units: percentage of subjects				
number (not applicable)				
Week 2	20.5	21.9		
Week 4	6.8	14.8		
Week 6	9.1	9.4		
Week 10	0	14.1		

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 119.4 days) + 14 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Adverse events reported in this group includes all subjects randomized the Placebo group during Weeks 1 - 20. Subjects who switched treatment at Week 10 were included in the other groups of the same dose for adverse events reported during Weeks 11 - 20.	
Reporting group title	GLPG0634 100 mg QD
Reporting group description:	
Adverse events reported in this group includes all subjects randomized to GLPG0634 100 mg QD during Weeks 11 -20.	
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 - 20. Subjects who switched treatment at Week 10 were included in the other groups of the same dose or placebo for adverse events reported during Weeks 11 - 20.	

Serious adverse events	Placebo	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 67 (4.48%)	2 / 52 (3.85%)	12 / 130 (9.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Infusion site thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 52 (1.92%)	0 / 130 (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			
Abdominal pain			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	2 / 130 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			

subjects affected / exposed	2 / 67 (2.99%)	2 / 52 (3.85%)	4 / 130 (3.08%)
occurrences causally related to treatment / all	1 / 2	1 / 2	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 67 (1.49%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 52 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	GLPG0634 100 mg QD	GLPG0634 200 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 67 (95.52%)	50 / 52 (96.15%)	118 / 130 (90.77%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 67 (14.93%)	5 / 52 (9.62%)	23 / 130 (17.69%)
occurrences (all)	31	18	38
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 67 (2.99%)	2 / 52 (3.85%)	10 / 130 (7.69%)
occurrences (all)	2	2	12
Fatigue			
subjects affected / exposed	0 / 67 (0.00%)	1 / 52 (1.92%)	7 / 130 (5.38%)
occurrences (all)	0	1	7
Influenza like illness			
subjects affected / exposed	4 / 67 (5.97%)	1 / 52 (1.92%)	3 / 130 (2.31%)
occurrences (all)	5	1	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 67 (2.99%)	3 / 52 (5.77%)	7 / 130 (5.38%)
occurrences (all)	6	3	8
Abdominal pain upper			
subjects affected / exposed	2 / 67 (2.99%)	0 / 52 (0.00%)	8 / 130 (6.15%)
occurrences (all)	2	0	10
Crohn's disease			
subjects affected / exposed	2 / 67 (2.99%)	4 / 52 (7.69%)	16 / 130 (12.31%)
occurrences (all)	2	4	16
Nausea			
subjects affected / exposed	1 / 67 (1.49%)	0 / 52 (0.00%)	11 / 130 (8.46%)
occurrences (all)	2	0	12
Vomiting			
subjects affected / exposed	2 / 67 (2.99%)	0 / 52 (0.00%)	7 / 130 (5.38%)
occurrences (all)	3	0	10
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	2 / 67 (2.99%)	3 / 52 (5.77%)	2 / 130 (1.54%)
occurrences (all)	3	3	2
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 67 (4.48%)	1 / 52 (1.92%)	7 / 130 (5.38%)
occurrences (all)	3	2	7
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 67 (2.99%)	3 / 52 (5.77%)	2 / 130 (1.54%)
occurrences (all)	2	3	2
Nasopharyngitis			
subjects affected / exposed	6 / 67 (8.96%)	4 / 52 (7.69%)	2 / 130 (1.54%)
occurrences (all)	6	4	2
Urinary tract infection			
subjects affected / exposed	5 / 67 (7.46%)	2 / 52 (3.85%)	5 / 130 (3.85%)
occurrences (all)	5	2	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 February 2014	General protocol amendment 1 to incorporate feedback, specific comments, and queries received from Competent Authorities and IECs. In particular, the definition for treatment failure was introduced, more stringent individual stopping criteria applied, and inclusion criteria modified. These changes were in line with the current treatment strategies for CD, beneficial for recruitment, and did not compromise subject safety. In addition, some clarifications and corrections were introduced in the study procedures.
08 August 2014	General protocol amendment 2, including: - an adjustment of the inclusion/exclusion criteria to better represent the current CD population without compromising the study objective. - an adjustment of the stratification factor related to previous anti-TNF exposure. - a refinement of general study procedures (removal of the urine drug Screening, addition of re-Screening and retesting, …) to provide further guidance to investigators. - an update of the background information on GLPG0634 and the benefit/risk section in accordance with the version of the IB current at the time (Edition 7.0, February 2014); this update included for example the results from a 39-week chronic toxicology study in dogs.
06 October 2014	General protocol amendment 3, including: - lower threshold for absolute lymphocyte counts for inclusion (inclusion criterion 9d) in order to be eligible for the study. - lower level of absolute lymphocyte counts required for urgent re-testing and discontinuation from treatment with the study medication and withdrawal from the study as listed in predefined individual stopping criteria (Section 10.2.3 of the clinical study protocol).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: