



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/m ² | | | |
| 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 histopathological 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 (\pm 1.91) | -3.5 (\pm 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 baseline | | | | |
| arithmetic mean (standard error) | 17.56 (\pm 5.085) | 33.82 (\pm 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 occurrences (all) | 2 / 67 (2.99%) 3 | 3 / 52 (5.77%) 3 | 2 / 130 (1.54%) 2 |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 3 / 67 (4.48%) 3 | 1 / 52 (1.92%) 2 | 7 / 130 (5.38%) 7 |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) | 2 / 67 (2.99%) 2 | 3 / 52 (5.77%) 3 | 2 / 130 (1.54%) 2 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 6 / 67 (8.96%) 6 | 4 / 52 (7.69%) 4 | 2 / 130 (1.54%) 2 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 5 / 67 (7.46%) 5 | 2 / 52 (3.85%) 2 | 5 / 130 (3.85%) 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: <ul style="list-style-type: none">- 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: <ul style="list-style-type: none">- 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: