



Clinical trial results:

A Phase 2, Randomized, Placebo-Controlled Trial Evaluating the Efficacy and Safety of Filgotinib in Subjects with Active Noninfectious Uveitis Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-001485-17 |
| Trial protocol | GB |
| Global end of trial date | 22 April 2021 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 11 January 2022 |
| First version publication date | 11 January 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-432-4097 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03207815 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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 | 22 April 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 December 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 April 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of filgotinib versus placebo for the treatment of the signs and symptoms of noninfectious uveitis as measured by the percentage of participants failing treatment for active noninfectious uveitis by Week 24.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 26 July 2017 |
| 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 | Australia: 1 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | New Zealand: 1 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | United States: 62 |
| Worldwide total number of subjects | 74 |
| EEA total number of subjects | 1 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| 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) | 66 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, the United Kingdom, Canada, Australia, Germany, Israel, and New Zealand. The first participant was screened on 26 July 2017. The last study visit occurred on 22 April 2021.

Pre-assignment

Screening details:

116 participants were screened.

Period 1

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

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Filgotinib |

Arm description:

Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Filgotinib |
| Investigational medicinal product code | |
| Other name | GS-6034, GLPG0634 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200 mg administered once daily

| | |
|--|--------------------|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg administered once on Day 1/Baseline

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

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

Dosage and administration details:

Administered once daily

| | |
|--|--------------------|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg administered once on Day 1/Baseline

| Number of subjects in period 1^[1] | Filgotinib | Placebo |
|---|------------|---------|
| Started | 37 | 35 |
| Completed | 30 | 29 |
| Not completed | 7 | 6 |
| Withdrew Consent | 1 | - |
| Adverse Event | 1 | 2 |
| Investigator's Discretion | 1 | 1 |
| Pregnancy/Partner Pregnancy | 1 | - |
| Protocol Violation | 2 | - |
| Lost to follow-up | 1 | 2 |
| Lack of efficacy | - | 1 |

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: 2 participants who were enrolled but not treated were not included in the disposition table.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Filgotinib |
|-----------------------|------------|

Reporting group description:

Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

| Reporting group values | Filgotinib | Placebo | Total |
|---|--------------|--------------|-------|
| Number of subjects | 37 | 35 | 72 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 48 ± 15.1 | 43 ± 15.7 | - |
| Gender categorical Units: Subjects | | | |
| Female | 23 | 20 | 43 |
| Male | 14 | 15 | 29 |
| Race Units: Subjects | | | |
| Asian | 4 | 0 | 4 |
| Black or African American | 2 | 8 | 10 |
| Native Hawaiian or Pacific Islander | 1 | 0 | 1 |
| White | 29 | 26 | 55 |
| Other | 1 | 1 | 2 |
| Ethnicity | | | |
| Not Permitted = local regulators did not allow collection of ethnicity information. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 10 | 14 |
| Not Hispanic or Latino | 32 | 25 | 57 |
| Not Permitted | 1 | 0 | 1 |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | Filgotinib |
| Reporting group description: Participants received filgotinib 200 milligrams (mg) tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15. | |

Primary: Percentage of Participants Failing Treatment for Active NonInfectious Uveitis by Week 24

| | |
|---|--|
| End point title | Percentage of Participants Failing Treatment for Active NonInfectious Uveitis by Week 24 |
| End point description: Treatment failure was a participant meeting at least 1 of these criteria in at least 1 eye: New active, inflammatory lesions relative to Day 1/Baseline (all visits starting Wk 6); Inability to achieve ≤Grade 0.5+ (at Wk 6)/2-step increase (change of Grade 0 to Grade 2+/Grade 0.5+ to Grade 3+) (all visits after Wk 6) relative to best state (RBS) achieved in Anterior Chamber (AC) cell grade (Standardization of Uveitis Nomenclature [SUN] criteria)[AC cell grades range from 0 (0 cells) to 4+ (>50 cells), higher scores=severe uveitis]; Inability to achieve ≤Grade 0.5+ (at Wk 6)/2-step increase (all visits after Wk 6) RBS achieved in Vitreous Haze (VH) grade (National Eye Institute [NEI]/SUN criteria)[VH grades range from 0(no evident VH) to 4+(optic nerve head is obscured), higher scores=severe uveitis]; Worsening of best corrected visual acuity (BCVA) by ≥15 letters RBS achieved (all visits starting Wk 6), measured by an eye chart, fewer correct letters=severe uveitis. Evaluable Analysis Set. | |
| End point type | Primary |
| End point timeframe: Week 6 through Week (Wk) 24 | |

| End point values | Filgotinib | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 37.5 (19.2 to 55.8) | 67.6 (50.5 to 84.8) | | |

Statistical analyses

| | |
|----------------------------|-----------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0064 ^[1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Treatment Failure Rate |
| Point estimate | -30.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -56.2 |
| upper limit | -4.1 |

Notes:

[1] - P-value was estimated from the Cochran-Mantel-Haenszel (CMH) test, adjusted for the stratification factors.

Secondary: Time to Treatment Failure on or After Week 6

| | |
|------------------------|---|
| End point title | Time to Treatment Failure on or After Week 6 |
| End point description: | Treatment failure was a participant meeting at least 1 of these criteria in at least 1 eye: New active, inflammatory lesions relative to Day 1/Baseline (all visits starting Wk 6); Inability to achieve ≤Grade 0.5+ (at Wk 6) or 2-step increase (change of Grade 0 to Grade 2+/Grade 0.5+ to Grade 3+) (all visits after Wk 6) relative to best state (RBS) achieved in AC cell grade (SUN criteria) [AC cell grades range from 0 (0 cells) to 4+ (>50 cells), higher scores=severe uveitis]; Inability to achieve ≤Grade 0.5+ (at Wk 6) or 2-step increase (all visits after Wk 6) RBS achieved in VH grade (NEI/SUN criteria) [VH grades range from 0 (no evident VH) to 4+ (optic nerve head is obscured), higher scores=severe uveitis]; Worsening of BCVA by ≥15 letters RBS achieved (all visits starting Wk 6), measured by an eye chart, fewer correct letters=severe uveitis. Participants in the Evaluable Analysis Set were analyzed. 9999=Not Available as the calculated percentiles of event rate were not reached. |
| End point type | Secondary |
| End point timeframe: | Week 6 through Week 52 |

| End point values | Filgotinib | Placebo | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: weeks | | | | |
| median (inter-quartile range (Q1-Q3)) | 9999 (24.1 to 9999) | 22.0 (12.1 to 47.0) | | |

Statistical analyses

| | |
|----------------------------|-----------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |

| | |
|---|--------------------------|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0014 ^[2] |
| Method | Stratified Log-Rank Test |
| Parameter estimate | Stratified Hazard Ratio |
| Point estimate | 0.309 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.144 |
| upper limit | 0.663 |

Notes:

[2] - P-value was derived from the log rank test stratified by the stratification factors.

Secondary: Change in Vitreous Haze (VH) Grade in Each Eye (NEI/SUN Criteria), From Best State Achieved Prior to Week 6 to Week 52 or End of Treatment (EOT) Visit or Early Termination (ET)

| | |
|-----------------|--|
| End point title | Change in Vitreous Haze (VH) Grade in Each Eye (NEI/SUN Criteria), From Best State Achieved Prior to Week 6 to Week 52 or End of Treatment (EOT) Visit or Early Termination (ET) |
|-----------------|--|

End point description:

Grading of VH was based on the publication from the NEI which has also been adapted by the SUN working group. VH grades range from 0 (no evident VH) to 4+ (optic nerve head is obscured), with higher scores indicating greater severity of uveitis. A negative change (cha) from the best value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

| End point values | Filgotinib | Placebo | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Left Eye: Best State Prior to Wk 6 N=32,33 | 0.3 (± 0.40) | 0.2 (± 0.33) | | |
| Right Eye: Best State Prior to Wk 6 | 0.3 (± 0.36) | 0.3 (± 0.45) | | |
| Lef Eye Cha From Best State at Wk52/EOT/ET N=32,33 | 0.1 (± 0.79) | 0.3 (± 0.75) | | |
| Rig Eye Cha From Best State at Wk52/EOT/ET N=32,33 | 0.1 (± 0.62) | 0.2 (± 0.66) | | |

Statistical analyses

| | |
|----------------------------|-----------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.355 ^[3] |
| Method | Repeated Measure ANCOVA |
| Parameter estimate | Least Squares Mean Treatment Difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 0.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.14 |

Notes:

[3] - P-value was estimated using a repeated measure Analysis of Covariance (ANCOVA) model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Change in Anterior Chamber (AC) Cell Grade in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

| | |
|-----------------|--|
| End point title | Change in Anterior Chamber (AC) Cell Grade in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET |
|-----------------|--|

End point description:

The number of AC cells observed within a 1 mm × 1 mm slit beam were recorded for each eye. The reported number was used to determine the grade according to the SUN criteria. AC cell grades range from 0 (0 cells in field) to 4+ (>50 cells in field), with higher scores indicating more cells visible in the AC and greater severity of uveitis. A negative change from the best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

| End point values | Filgotinib | Placebo | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Left Eye: Best State Prior to Wk 6 | 0.0 (± 0.09) | 0.1 (± 0.19) | | |
| Right Eye: Best State Prior to Wk 6 | 0.0 (± 0.12) | 0.1 (± 0.25) | | |
| Left Eye: Change From Best State at Wk 52/EOT/ET | 0.2 (± 0.59) | 0.6 (± 0.87) | | |
| Right Eye: Change From Best State at Wk 52/EOT/ET | 0.2 (± 0.53) | 0.7 (± 1.05) | | |

Statistical analyses

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0145 ^[4] |
| Method | Repeated Measure ANCOVA |
| Parameter estimate | LS Mean Treatment Difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | -0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.18 |

Notes:

[4] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Change in Logarithm of the Minimal Angle of Resolution (logMAR) Best Corrected Visual Acuity (BCVA) in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

| | |
|-----------------|---|
| End point title | Change in Logarithm of the Minimal Angle of Resolution (logMAR) Best Corrected Visual Acuity (BCVA) in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET |
|-----------------|---|

End point description:

BCVA is the best possible vision that an eye can achieve with the set of glasses or contact lenses. A refraction test was performed to measure the appropriate lens strength to focus light on the retina. Using the appropriate corrective lenses based on that visit's refraction, participant's BCVA was measured using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart. In the ETDRS system, 15 letters is equal to a change in 3 lines of visual acuity. If the participant is unable to read letters on a testing chart, visual acuity is described as ranging from ability to count fingers, recognize hand movements, or light perception. The smaller BVCA score indicates greater severity of uveitis. A positive change from best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

| End point values | Filgotinib | Placebo | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: logMAR | | | | |
| arithmetic mean (standard deviation) | | | | |
| Left Eye: Best State Prior to Wk 6 | 0.09 (± 0.195) | 0.07 (± 0.209) | | |
| Right Eye: Best State Prior to Wk 6 | 0.09 (± 0.193) | 0.12 (± 0.280) | | |
| Left Eye: Change From Best State at Wk 52/EOT/ET | 0.03 (± 0.154) | 0.05 (± 0.112) | | |
| Right Eye: Change From Best State at Wk 52/EOT/ET | -0.01 (± 0.116) | 0.07 (± 0.144) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0389 ^[5] |
| Method | Repeated Measure ANCOVA |
| Parameter estimate | LS Mean Treatment Difference |
| Point estimate | -0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.025 |

Notes:

[5] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, stratification factors and best state value.

Secondary: Log Change in Central Retinal Thickness in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET

| | |
|-----------------|---|
| End point title | Log Change in Central Retinal Thickness in Each Eye, From Best State Achieved Prior to Week 6 to Week 52 or EOT Visit or ET |
|-----------------|---|

End point description:

Central retinal thickness is measured by optical coherence tomography (OCT). Central retinal thickness is defined as the thickness of the retina in the center of the foveal pit (1 mm subfield). The larger central retinal thickness value indicates greater severity of uveitis. A negative change (cha) from best state value obtained prior to Week 6 indicates improvement. Participants in the Evaluable Analysis Set with the available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Prior to Week 6; Up to Week 52 or EOT or ET (maximum: 53 weeks)

| End point values | Filgotinib | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: log microns | | | | |
| arithmetic mean (standard deviation) | | | | |
| Left Eye: Best State Prior to Wk 6 | 2.45 (± 0.059) | 2.46 (± 0.097) | | |
| Right Eye: Best State Prior to Wk 6 | 2.47 (± 0.056) | 2.44 (± 0.104) | | |

| | | | | |
|--|---------------------|---------------------|--|--|
| Lef Eye Cha From Best State at Wk52/EOT/ET N=32,32 | 0.01 (\pm 0.062) | 0.04 (\pm 0.080) | | |
| Rig Eye Cha From Best State at Wk52/EOT/ET N=32,32 | 0.01 (\pm 0.049) | 0.03 (\pm 0.055) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.034 ^[6] |
| Method | Repeated Measure ANCOVA |
| Parameter estimate | LS Mean Treatment Difference |
| Point estimate | -0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | 0 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.011 |

Notes:

[6] - P-value was estimated using a repeated measure ANCOVA model which included treatment, eye, interaction of treatment and eye, OCT machine, and best state value.

Secondary: Time to Development of Macular Edema in At Least One Eye on or After Week 6

| | |
|------------------------|--|
| End point title | Time to Development of Macular Edema in At Least One Eye on or After Week 6 |
| End point description: | Time in weeks until the development of Macular edema or Week 52 or EOT or ET. Macular edema is determined by OCT and is defined as central retinal thickness \geq 300 microns if using Cirrus machine, or \geq 315 microns if using Spectralis machine. Participants in the Evaluable Analysis Set were analyzed. 9999=Not Available as the calculated percentiles of event rate were not reached. |
| End point type | Secondary |
| End point timeframe: | Week 6 through Week 52 |

| | | | | |
|---------------------------------------|-------------------|--------------------|--|--|
| End point values | Filgotinib | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 34 | | |
| Units: weeks | | | | |
| median (inter-quartile range (Q1-Q3)) | 7.8 (6.1 to 9999) | 12.3 (6.1 to 9999) | | |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Filgotinib vs Placebo |
| Comparison groups | Filgotinib v Placebo |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5893 ^[7] |
| Method | Stratified Log-Rank Test |
| Parameter estimate | Stratified Hazard Ratio |
| Point estimate | 1.193 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.625 |
| upper limit | 2.277 |

Notes:

[7] - P-value was derived from the log rank test stratified by the stratification factors.

Secondary: Plasma Concentration of Filgotinib

| | |
|------------------------|---|
| End point title | Plasma Concentration of Filgotinib ^[8] |
| End point description: | Participants in the Safety Analysis Set who have at least one non-missing concentration data with available data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Day 1 post dose, Weeks 4 and 6 predose, Week 12 post dose, Weeks 24, 36, 52 (EOT), Early Termination at any time |

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Plasma concentrations were collected and analyzed for filgotinib arm group.

| End point values | Filgotinib | | | |
|---|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 37 | | | |
| Units: nanograms per millilitre (ng/ml) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 Postdose | 748.5 (± 1043.84) | | | |
| Week 4 Predose (N=29) | 173.3 (± 364.46) | | | |
| Week 6 Predose (N=28) | 133.9 (± 306.18) | | | |
| Week 12 Postdose (N=27) | 1088.7 (± 856.57) | | | |

| | | | | |
|--|------------------|--|--|--|
| Week 24 Single Anytime (N=21) | 397.5 (± 561.57) | | | |
| Week 36 Single Anytime (N=14) | 295.7 (± 420.25) | | | |
| Week 52 (EOT) Single Anytime (N=22) | 195.2 (± 344.54) | | | |
| Early Termination Single Anytime (N=3) | 434.8 (± 478.72) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Metabolite, GS-829845

| | |
|-----------------|--|
| End point title | Plasma Concentration of Metabolite, GS-829845 ^[9] |
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End point description:

Participants in the Safety Analysis Set who have at least one non-missing concentration data with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 post dose, Weeks 4 and 6 predose, Week 12 post dose, Weeks 24, 36, 52 (EOT), Early Termination at any time

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Plasma concentrations were collected and analyzed for filgotinib arm group.

| End point values | Filgotinib | | | |
|--|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 37 | | | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 Postdose | 230.8 (± 317.98) | | | |
| Week 4 Predose (N=29) | 2085.6 (± 924.91) | | | |
| Week 6 Predose (N=28) | 2107.7 (± 749.28) | | | |
| Week 12 Postdose (N=27) | 3237.0 (± 1180.74) | | | |
| Week 24 Single Anytime (N=21) | 3478.1 (± 1137.63) | | | |
| Week 36 Single Anytime (N=14) | 2944.3 (± 1130.84) | | | |
| Week 52 (EOT) Single Anytime (N=22) | 2510.7 (± 1732.59) | | | |
| Early Termination Single Anytime (N=3) | 2171.0 (± 1224.77) | | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to 30 days after the last dose of study drug (maximum exposure up to 57 weeks); All-Cause Mortality: From randomization up to 57 weeks

Adverse event reporting additional description:

Adverse Events: Safety Analysis Set included all participants who received at least 1 dose of study drug. All- Cause Mortality: All Randomized Analysis Set included all participants who were randomized in the study.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|--------------------|------|
| Dictionary version | 24.0 |
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Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Filgotinib |
|-----------------------|------------|

Reporting group description:

Participants received filgotinib 200 mg tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo to match filgotinib tablet orally, once daily for up to 52 weeks along with a standardized prednisone burst of 60 mg/day at Day 1/Baseline followed by a protocol-defined mandatory taper schedule up to Week 15.

| Serious adverse events | Filgotinib | Placebo | |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 37 (13.51%) | 2 / 35 (5.71%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Retinal vasculitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 35 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uveitis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Inflammatory bowel disease | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Bladder prolapse | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Spinal stenosis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Covid-19 | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 35 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 35 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| Non-serious adverse events | Filgotinib | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 37 (75.68%) | 19 / 35 (54.29%) | |
| Investigations | | | |
| Intraocular pressure increased | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) | |
| occurrences (all) | 2 | 2 | |
| Weight increased | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 35 (2.86%) | |
| occurrences (all) | 3 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 0 / 35 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 35 (8.57%) | |
| occurrences (all) | 2 | 3 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 7 / 35 (20.00%) | |
| occurrences (all) | 4 | 7 | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 0 / 35 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 3 / 35 (8.57%) | |
| occurrences (all) | 3 | 3 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 4 / 35 (11.43%) | |
| occurrences (all) | 2 | 4 | |
| Visual impairment | | | |
| subjects affected / exposed | 5 / 37 (13.51%) | 1 / 35 (2.86%) | |
| occurrences (all) | 5 | 1 | |

| | | |
|-------------------------------|----------------|----------------|
| Chorioretinal disorder | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) |
| occurrences (all) | 2 | 2 |
| Eye irritation | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) |
| occurrences (all) | 2 | 2 |
| Uveitis | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) |
| occurrences (all) | 2 | 2 |
| Vitreous floaters | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 35 (2.86%) |
| occurrences (all) | 3 | 1 |
| Anterior chamber inflammation | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 35 (5.71%) |
| occurrences (all) | 1 | 2 |
| Cataract | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 1 |
| Eye pain | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 1 |
| Macular oedema | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 1 |
| Photopsia | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 0 / 35 (0.00%) |
| occurrences (all) | 3 | 0 |
| Chalazion | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 2 |
| Ocular hyperaemia | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 |
| Photophobia | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 |

| | | | |
|---|----------------------|----------------------|--|
| Vitreous haze subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 35 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 1 / 35 (2.86%) 1 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 0 / 35 (0.00%) 0 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 2 / 35 (5.71%) 2 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 3 / 37 (8.11%) 3 | 1 / 35 (2.86%) 1 | |
| Abdominal distension subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 35 (0.00%) 0 | |
| Constipation subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 35 (0.00%) 0 | |
| Dry mouth subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 35 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Upper-airway cough syndrome subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 2 / 35 (5.71%) 2 | |
| Sleep apnoea syndrome subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 35 (0.00%) 0 | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 4 / 35 (11.43%) 4 | |

| | | | |
|---|-----------------|----------------|--|
| Anxiety | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) | |
| occurrences (all) | 2 | 2 | |
| Depression | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 1 / 35 (2.86%) | |
| occurrences (all) | 2 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 35 (5.71%) | |
| occurrences (all) | 4 | 2 | |
| Back pain | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 35 (2.86%) | |
| occurrences (all) | 3 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 35 (5.71%) | |
| occurrences (all) | 2 | 2 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 35 (5.71%) | |
| occurrences (all) | 1 | 2 | |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 35 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 35 (5.71%) | |
| occurrences (all) | 0 | 2 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 3 / 35 (8.57%) | |
| occurrences (all) | 6 | 3 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 35 (5.71%) | |
| occurrences (all) | 3 | 3 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 35 (5.71%) | |
| occurrences (all) | 1 | 2 | |
| Covid-19 | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 35 (0.00%) | |
| occurrences (all) | 2 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 14 November 2017 | <ul style="list-style-type: none">• ECG collection at the Screening visit only.• Allowed for the safety laboratory assessments to be performed locally or centrally at Screening visit only.• Removed lens photography and reduced fundus photography assessments.• Removed sarcoidosis assessments and sarcoidosis imaging requirements.• Clarified requirements for Unscheduled visits related to uveitis symptoms.• Updated Inclusion criteria to clarify oral corticosteroid requirements prior to Day 1 dosing.• Updated Exclusion criteria to clarify severe glaucoma.• Updated Inclusion criteria to clarify QuantiFERON® TB Gold and TB testing requirements.• Updated Exclusion criteria to clarify immunosuppressive therapy.• Updated Exclusion criteria to clarify concomitant immunosuppressive therapy.• Updated Exclusion criteria to exclude eyelid surgery from prior ocular surgery.• Updated Exclusion criteria to exclude eyelid surgery from planned (elective) eye surgery.• Updated Exclusion criteria to clarify HIV and Syphilis testing requirements.• Updated Exclusion criteria to define marijuana and tobacco use.• Updated storage and handling conditions for filgotinib.• Updated tonometry requirements.• Updated Fluorescein Angiogram requirements.• Updated risk/benefit assessment language.• Updated study drug return or disposal language.• Updated study schema.• Updated prohibited medications.• Updated study title.• Updated pregnancy precautions, definition for female of childbearing potential, and contraceptive requirements.• Updated clinical laboratory assessment table.• Updated references.• Added Ct.gov NCT number. |
| 18 December 2017 | <ul style="list-style-type: none">• Updated synopsis, study design to correct inconsistencies made when incorporating changes into protocol amendment 1.• Updated synopsis and main eligibility criteria to correct inconsistencies between changes outlined in the summary of changes document and protocol amendment 1.• Updated synopsis, study procedures/frequency to delete lipid profile from screening.• Updated Inclusion criteria to correct inconsistencies made when incorporating changes into protocol amendment 1.• Updated subscripts to provide clarity around HBV Viral Monitoring and also, childbearing potential.• Updated to clarify the definition of childbearing potential. |
| 12 December 2019 | <ul style="list-style-type: none">• Relaxation of entry criteria to allow participants that have previously failed anti-TNF treatment.• Relaxation of entry criteria to allow participants with previously treated active or latent TB.• DSPH (Drug Safety and Public Health) was replaced by PVE (Pharmacovigilance & Epidemiology) within the whole document. |

| | |
|---------------|---|
| 17 March 2020 | <ul style="list-style-type: none"> • Expand the sample size to N = 248 participants. • Expand the number of sites globally to approximately 75 centers. • Incorporate an independent adjudication committee to review major adverse cardiovascular events and thromboembolic events. • Add a new study drug discontinuation criterion: any thromboembolic events meeting serious adverse event (SAE) reporting criteria. • Language regarding independent adjudication committee reviews for major adverse cardiovascular events and thromboembolic events has been updated throughout the protocol. |
|---------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---------------|---|--------------|
| 20 March 2020 | There were global interruptions to enrollment due to corona virus disease 2019 (COVID-19) outbreak, measures were taken to introduce a global screening halt. Decision to restart enrolment was made on data monitoring committee (DMC) recommendation. | 21 May 2020 |

Notes:

Limitations and caveats

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

Study was terminated early due to termination of the development program. Due to early termination and small sample size, PK analysis was not performed for this study.

Notes: