



Clinical trial results:

Evaluation of the Efficacy and Safety of GS-5745 as Add-On Therapy to a Tumor Necrosis Factor Inhibitor and Methotrexate Regimen in Subjects with Moderate to Severe Rheumatoid Arthritis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-000897-39 |
| Trial protocol | HU DE BE |
| Global end of trial date | 07 August 2017 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 16 June 2018 |
| First version publication date | 16 June 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-373-1499 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02862574 |
| 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 | 07 August 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 June 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 August 2017 |
| 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 andecaliximab (GS-5745) versus placebo as an add-on therapy to a tumor necrosis factor (TNF) inhibitor and methotrexate in adults with moderate to severe rheumatoid arthritis (RA).

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:

Participants remained on their current treatment regimen of a TNF inhibitor and methotrexate.

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 December 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 15 |
| Worldwide total number of subjects | 15 |
| EEA total number of subjects | 0 |

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) | 13 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States. The first participant was screened on 15 December 2016. The last study visit occurred on 07 August 2017.

Pre-assignment

Screening details:

28 participants were screened.

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | Double-Blind Treatment 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 | Andecaliximab 300 mg |
|------------------|----------------------|

Arm description:

Andecaliximab 300 mg for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Andecaliximab |
| Investigational medicinal product code | |
| Other name | GS-5745 |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg administered once weekly

| | |
|------------------|----------------------|
| Arm title | Andecaliximab 150 mg |
|------------------|----------------------|

Arm description:

Andecaliximab 150 mg + placebo for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Andecaliximab |
| Investigational medicinal product code | |
| Other name | GS-5745 |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150 mg administered once weekly

| | |
|--|--|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered once weekly

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

Arm description:

Placebo once weekly for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered once weekly

| Number of subjects in period 1 | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo |
|---------------------------------------|----------------------|----------------------|---------|
| Started | 5 | 5 | 5 |
| Completed | 2 | 3 | 1 |
| Not completed | 3 | 2 | 4 |
| Adverse event, non-fatal | - | 1 | - |
| Study Terminated by Sponsor | 3 | 1 | 4 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open-Label Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Andecaliximab 300 mg to Andecaliximab 300 mg |

Arm description:

Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Andecaliximab |
| Investigational medicinal product code | |
| Other name | GS-5745 |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

300 mg administered once weekly

| | |
|------------------|--|
| Arm title | Andecaliximab 150 mg to Andecaliximab 300 mg |
|------------------|--|

Arm description:

Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | Andecaliximab |
| Investigational medicinal product code | |
| Other name | GS-5745 |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150 mg administered once weekly

| | |
|--|--|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered once weekly

| | |
|------------------|---------------------------------|
| Arm title | Placebo to Andecaliximab 300 mg |
|------------------|---------------------------------|

Arm description:

Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered once weekly

| Number of subjects in period 2 | Andecaliximab 300 mg to Andecaliximab 300 mg | Andecaliximab 150 mg to Andecaliximab 300 mg | Placebo to Andecaliximab 300 mg |
|---------------------------------------|--|--|---------------------------------|
| Started | 2 | 3 | 1 |
| Completed | 0 | 0 | 0 |
| Not completed | 2 | 3 | 1 |
| Study Terminated by Sponsor | 2 | 3 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | Andecaliximab 300 mg |
| Reporting group description: Andecaliximab 300 mg for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Andecaliximab 150 mg |
| Reporting group description: Andecaliximab 150 mg + placebo for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Placebo |
| Reporting group description: Placebo once weekly for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |

| Reporting group values | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo |
|------------------------------------|----------------------|----------------------|---------|
| Number of subjects | 5 | 5 | 5 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| Age continuous Units: years arithmetic mean standard deviation | 54 ± 16.3 | 57 ± 9.3 | 58 ± 5.6 |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 4 | 4 |
| Male | 2 | 1 | 1 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 0 | 2 | 0 |
| Not Hispanic or Latino | 5 | 3 | 5 |
| Race Units: Subjects | | | |
| White | 3 | 5 | 4 |
| Black | 2 | 0 | 1 |
| Disease Activity Score Creactive Protein (DAS28(CRP)) | | | |
| The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and C-Reactive Protein (CRP) for a total possible score of 2 to 10. Higher values indicate higher disease activity. | | | |
| Units: units on a scale arithmetic mean standard deviation | 5.79 ± 0.814 | 5.90 ± 0.752 | 5.69 ± 0.887 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 15 | | |

| | | | |
|--|----|--|--|
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 11 | | |
| Male | 4 | | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 2 | | |
| Not Hispanic or Latino | 13 | | |
| Race Units: Subjects | | | |
| White | 12 | | |
| Black | 3 | | |
| Disease Activity Score Creactive Protein (DAS28(CRP)) | | | |
| The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and C-Reactive Protein (CRP) for a total possible score of 2 to 10. Higher values indicate higher disease activity. | | | |
| Units: units on a scale arithmetic mean standard deviation | - | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Andecaliximab 300 mg |
| Reporting group description: Andecaliximab 300 mg for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Andecaliximab 150 mg |
| Reporting group description: Andecaliximab 150 mg + placebo for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Placebo |
| Reporting group description: Placebo once weekly for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Andecaliximab 300 mg to Andecaliximab 300 mg |
| Reporting group description: Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Andecaliximab 150 mg to Andecaliximab 300 mg |
| Reporting group description: Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |
| Reporting group title | Placebo to Andecaliximab 300 mg |
| Reporting group description: Andecaliximab 300 mg for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate | |

Primary: Change From Baseline in DAS28(CRP) at Week 12

| | |
|--|--|
| End point title | Change From Baseline in DAS28(CRP) at Week 12 ^[1] |
| End point description: The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and CRP for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. A negative change from baseline indicates improvement. Participants in the Full Analysis Set (all randomized participants who received at least 1 dose of study drug) with available data were analyzed. | |
| End point type | Primary |
| End point timeframe: Baseline; Week 12 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical comparison was planned or performed.

| End point values | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo | |
|--------------------------------------|-------------------------|-------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2 | 3 | 3 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 0.13 (\pm 0.115) | -1.51 (\pm 0.670) | -0.36 (\pm 0.353) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants That Achieve DAS28(CRP) \leq 3.2 at Week 12

| | |
|--|--|
| End point title | Percentage of Participants That Achieve DAS28(CRP) \leq 3.2 at Week 12 |
| End point description: The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and CRP for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. A negative change from baseline indicates improvement. Participants in the Full Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: Week 12 | |

| End point values | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo | |
|-----------------------------------|-------------------------|-------------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 5 | 5 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants That Achieve DAS28(CRP) $<$ 2.6 at Week 12

| | |
|--|---|
| End point title | Percentage of Participants That Achieve DAS28(CRP) $<$ 2.6 at Week 12 |
| End point description: The DAS28 score is a measure of the participant's disease activity calculated using the tender joint counts (28 joints), swollen joint counts (28 joints), Patient's Global Assessment of Disease Activity (visual analog scale: 0 = no disease activity to 100 = maximum disease activity), and CRP for a total possible score of 1 to 9.4. Higher values indicate higher disease activity. A negative change from baseline indicates improvement. Participants in the Full Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: Week 12 | |

| End point values | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo | |
|-----------------------------------|-------------------------|-------------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 5 | 5 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Andecaliximab

| | |
|------------------------|--|
| End point title | Plasma Concentration of Andecaliximab |
| End point description: | The plasma concentrations of andecaliximab were not collected and were not analyzed. |
| End point type | Secondary |
| End point timeframe: | |
| Day 4 or 6 (± 1 day) | |

| End point values | Andecaliximab 300 mg | Andecaliximab 150 mg | Placebo | |
|--------------------------------------|-------------------------|-------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | 0 ^[4] | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

[2] - The plasma concentrations of andecaliximab were not collected and were not analyzed.

[3] - The plasma concentrations of andecaliximab were not collected and were not analyzed.

[4] - The plasma concentrations of andecaliximab were not collected and were not analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to the last dose date (maximum: 127 days) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set: participants who received at least 1 dose of study drug

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Andecaliximab 300 mg (Double-Blind) |
|-----------------------|-------------------------------------|

Reporting group description:

Andecaliximab 300 mg for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Andecaliximab 150 mg (Double-Blind) |
|-----------------------|-------------------------------------|

Reporting group description:

Andecaliximab 150 mg + placebo for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|-----------------------|------------------------|
| Reporting group title | Placebo (Double-Blind) |
|-----------------------|------------------------|

Reporting group description:

Placebo once weekly for 12 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Andecaliximab 300 mg (Open-Label) |
|-----------------------|-----------------------------------|

Reporting group description:

Andecaliximab 300 mg administered via subcutaneous injection once weekly for up to 52 weeks, in addition to participant's current regimen of a TNF inhibitor and methotrexate

| Serious adverse events | Andecaliximab 300 mg (Double-Blind) | Andecaliximab 150 mg (Double-Blind) | Placebo (Double-Blind) |
|---|-------------------------------------|-------------------------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 5 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Andecaliximab 300 mg (Open-Label) | | |
|---|-----------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | | |

| | | | |
|---|----------------|--|--|
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Reproductive system and breast disorders | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Andecaliximab 300 mg (Double-Blind) | Andecaliximab 150 mg (Double-Blind) | Placebo (Double-Blind) |
|---|--|--|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 5 (60.00%) | 2 / 5 (40.00%) | 2 / 5 (40.00%) |
| Investigations | | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fractured sacrum | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---|--|---|
| Skin and subcutaneous tissue disorders Rash papular subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 5 (20.00%) 1 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 | 1 / 5 (20.00%) 1 0 / 5 (0.00%) 0 |

| | | | |
|--|-----------------------------------|--|--|
| Non-serious adverse events | Andecaliximab 300 mg (Open-Label) | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 2 / 6 (33.33%) | | |
| Investigations White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Fractured sacrum subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| Nervous system disorders Headache | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 | | |
| Skin and subcutaneous tissue disorders Rash papular subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 24 June 2016 | Amendment #1 was initiated to add study drug administration visits to the Schedule of Assessments and to eliminate an un-needed visit. Several points were clarified and several clerical errors were corrected such as biomarker collection time-points. |
| 23 September 2016 | The following changes were made to enhance safety monitoring: <ul style="list-style-type: none">• Added chest x-ray at screening to further exclude active TB or lung disease and annually to monitor for re-activation of disease• Added annual QuantiFERON-TB Gold test to monitor for re-activation of tuberculosis (TB)• Added reflex testing for Hepatitis B and C every 3 months if subjects test positive for serology at screening• Added erythrocyte sedimentation rate (ESR) at all study visits to correlate sedimentation rates with C-Reactive protein (CRP) levels• Added pregnancy precaution requirements for methotrexate (MTX)• Added additional hematology and chemistry lab draws at Open Label Extension (OLE) weeks 19, 30, 42, and 54 to monitor for infection. Additional instructions were added for potential re-screening of eligible subjects |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|---|--------------|
| 06 June 2017 | Gilead made a decision to discontinue the development of andecaliximab in rheumatoid arthritis. This decision was not due to any safety concerns with andecaliximab or with study procedures. As a result of the decision, Study GS-US-373-1499 was terminated. | - |

Notes:

Limitations and caveats

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

Because the study was terminated early by the sponsor and only 15 participants were enrolled, no formal statistical testing was completed for the final analysis.

Notes: