



Clinical trial results:

A Phase 2, Blinded, Randomized, Placebo-Controlled Study Evaluating the Efficacy and Safety of GS-4875 in Subjects with Moderately to Severely Active Ulcerative Colitis

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2019-001430-33 |
| Trial protocol | AT FR GB DE PL BE IT |
| Global end of trial date | 14 December 2021 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 14 August 2022 |
| First version publication date | 14 August 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-365-4237 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04130919 |
| 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 | 14 December 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 February 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 December 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the efficacy of tilpisertib (formerly GS-4875) compared with placebo control in achieving clinical remission per modified Mayo Clinic Score (MCS) in adults with moderately to severely active ulcerative colitis (UC).

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 | 20 December 2019 |
| 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: 3 |
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Switzerland: 3 |
| Country: Number of subjects enrolled | United States: 10 |
| Worldwide total number of subjects | 19 |
| EEA total number of subjects | 3 |

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) | 15 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Europe and the United States.

Pre-assignment

Screening details:

32 participants were screened.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Blinded Treatment Phase |
| 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 | Tilpisertib 300 mg (Blinded Treatment Phase) |

Arm description:

Tilpisertib 300 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per Modified Mayo Clinic score (MCS) at Week 10, continued to receive tilpisertib 300 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|----------------------------------------|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tilpisertib |
| Investigational medicinal product code | |
| Other name | GS-4875 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg administered once daily

| | |
|------------------|----------------------------------------------|
| Arm title | Tilpisertib 100 mg (Blinded Treatment Phase) |
|------------------|----------------------------------------------|

Arm description:

Tilpisertib 100 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive tilpisertib 100 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|----------------------------------------|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tilpisertib |
| Investigational medicinal product code | |
| Other name | GS-4875 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg administered once daily

| | |
|------------------|-----------------------------------|
| Arm title | Placebo (Blinded Treatment Phase) |
|------------------|-----------------------------------|

Arm description:

Placebo tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive placebo tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|----------|---------|
| 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: | |
| Administered once daily | |

| Number of subjects in period 1 | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) |
|--------------------------------|-------------------------------------------------|-------------------------------------------------|-----------------------------------|
| Started | 7 | 6 | 6 |
| Completed | 5 | 4 | 3 |
| Not completed | 2 | 2 | 3 |
| Investigator's decision | - | 1 | - |
| Adverse event, non-fatal | - | - | 1 |
| Study terminated by sponsor | 1 | 1 | 1 |
| Disease worsening | - | - | 1 |
| Withdrew consent | 1 | - | - |

Period 2

| | |
|------------------------------|----------------------------|
| Period 2 title | Open-label Treatment Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Tilpisertib 300 mg from Tilpisertib 300 mg (OLTP) |

Arm description:

Participants who received tilpisertib 300 mg and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| | |
|----------------------------------------|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tilpisertib |
| Investigational medicinal product code | |
| Other name | GS-4875 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg administered once daily

| | |
|------------------|---------------------------------------------------|
| Arm title | Tilpisertib 300 mg from Tilpisertib 100 mg (OLTP) |
|------------------|---------------------------------------------------|

Arm description:

Participants who received tilpisertib 100 mg and did not achieve clinical response per modified MCS at

Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| | |
|----------------------------------------|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tilpisertib |
| Investigational medicinal product code | |
| Other name | GS-4875 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg administered once daily

| | |
|------------------|----------------------------------------|
| Arm title | Tilpisertib 300 mg from Placebo (OLTP) |
|------------------|----------------------------------------|

Arm description:

Participants who received placebo and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| | |
|----------------------------------------|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tilpisertib |
| Investigational medicinal product code | |
| Other name | GS-4875 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg administered once daily

| Number of subjects in period 2^[1] | Tilpisertib 300 mg from Tilpisertib 300 mg (OLTP) | Tilpisertib 300 mg from Tilpisertib 100 mg (OLTP) | Tilpisertib 300 mg from Placebo (OLTP) |
|-----------------------------------------------------|---------------------------------------------------|---------------------------------------------------|----------------------------------------|
| Started | 4 | 3 | 3 |
| Completed | 1 | 1 | 0 |
| Not completed | 3 | 2 | 3 |
| Investigator's decision | 1 | - | - |
| Disease worsening | 1 | - | 1 |
| Withdrew consent | 1 | 1 | 1 |
| Lost to follow-up | - | - | 1 |
| MCS response not achieved at open-label week 10 | - | 1 | - |

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: Participants who completed the Blinded Treatment phase and did not achieve the clinical response per modified MCS at Week 10 entered in Open-label Treatment phase to receive tilpisertib 300 mg.

Baseline characteristics

Reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Reporting group title | Tilpisertib 300 mg (Blinded Treatment Phase) |
| Reporting group description: | |
| Tilpisertib 300 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per Modified Mayo Clinic score (MCS) at Week 10, continued to receive tilpisertib 300 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |
| Reporting group title | Tilpisertib 100 mg (Blinded Treatment Phase) |
| Reporting group description: | |
| Tilpisertib 100 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive tilpisertib 100 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |
| Reporting group title | Placebo (Blinded Treatment Phase) |
| Reporting group description: | |
| Placebo tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive placebo tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |

| Reporting group values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) |
|------------------------|-------------------------------------------------|-------------------------------------------------|-----------------------------------|
| Number of subjects | 7 | 6 | 6 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|-----------------------------------------------------------------------------------------|--------|--------|--------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 51 | 49 | 43 |
| standard deviation | ± 11.8 | ± 22.6 | ± 18.4 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 1 | 3 |
| Male | 5 | 5 | 3 |
| Race | | | |
| Not Permitted means local regulators did not allow collection of race information. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 7 | 6 | 3 |
| Other | 0 | 0 | 1 |
| Not Permitted | 0 | 0 | 0 |
| Ethnicity | | | |
| Not Permitted means local regulators did not allow collection of ethnicity information. | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 6 | 4 | 6 |
| Hispanic or Latino | 1 | 2 | 0 |
| Not Permitted | 0 | 0 | 0 |

| | | | |
|-----------------------------------------------------------------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 19 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | | |
| Male | 13 | | |
| Race | | | |
| Not Permitted means local regulators did not allow collection of race information. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Black or African American | 2 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| White | 16 | | |
| Other | 1 | | |
| Not Permitted | 0 | | |
| Ethnicity | | | |
| Not Permitted means local regulators did not allow collection of ethnicity information. | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 16 | | |
| Hispanic or Latino | 3 | | |
| Not Permitted | 0 | | |

End points

End points reporting groups

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Reporting group title | Tilpisertib 300 mg (Blinded Treatment Phase) |
| Reporting group description: Tilpisertib 300 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per Modified Mayo Clinic score (MCS) at Week 10, continued to receive tilpisertib 300 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |
| Reporting group title | Tilpisertib 100 mg (Blinded Treatment Phase) |
| Reporting group description: Tilpisertib 100 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive tilpisertib 100 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |
| Reporting group title | Placebo (Blinded Treatment Phase) |
| Reporting group description: Placebo tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive placebo tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase. | |
| Reporting group title | Tilpisertib 300 mg from Tilpisertib 300 mg (OLTP) |
| Reporting group description: Participants who received tilpisertib 300 mg and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP). | |
| Reporting group title | Tilpisertib 300 mg from Tilpisertib 100 mg (OLTP) |
| Reporting group description: Participants who received tilpisertib 100 mg and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP). | |
| Reporting group title | Tilpisertib 300 mg from Placebo (OLTP) |
| Reporting group description: Participants who received placebo and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP). | |

Primary: Percentage of Participants who Achieved Clinical Remission per Modified Mayo Clinic Score (MCS) at Week 10

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved Clinical Remission per Modified Mayo Clinic Score (MCS) at Week 10 ^[1] |
| End point description: The modified MCS is a scoring system for assessment of ulcerative colitis (UC) activity and is composed of subscores from endoscopy (range: 0 to 3, where 0 = normal or inactive disease and 3 = severe disease [spontaneous bleeding, ulceration]), rectal bleeding (range: 0 to 3, where 0 = no blood seen and 3 = blood alone passes), stool frequency (range: 0 to 3, where 0 = normal number of stools and 3 = at least 5 or more stools more than normal), and physician's global assessment (PGA) (range: 0 to 3, where 0 = normal and 3 = severe disease). Total score for MCS ranges from 0 to 12 (sum of all subscores), with higher scores indicating higher disease activity. Clinical remission per modified MCS is defined as stool frequency subscore ≤ 1 and not greater than baseline, rectal bleeding subscore of 0, and endoscopic subscore ≤ 1 at Week 10. Full analysis set included all randomized participants who received at least 1 dose of study drug. | |
| End point type | Primary |
| End point timeframe: Week 10 | |

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 formal statistical hypotheses were tested for the primary end point.

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 7 | 6 | 6 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Endoscopic Response at Week 10

| | |
|-----------------|------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved Endoscopic Response at Week 10 |
|-----------------|------------------------------------------------------------------------|

End point description:

Endoscopic response was defined as an endoscopic subscore of ≤ 1 at Week 10. Endoscopic subscore is a part of the modified MCS which is a scoring system for assessment of UC activity. Endoscopic subscore range: 0 to 3, where 0 = normal or inactive disease, 1 = mild disease (erythema, decreased vascular pattern), 2 = moderate disease (marked erythema, lack of vascular pattern, friability, erosions), and 3 = severe disease (spontaneous bleeding, ulceration). Participants in the Full Analysis Set were analyzed.

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

End point timeframe:

Week 10

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 7 | 6 | 6 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 14.3 | 16.7 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved MCS Response at Week 10

| | |
|-----------------|-----------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved MCS Response at Week 10 |
|-----------------|-----------------------------------------------------------------|

End point description:

The modified MCS is a scoring system for assessment of UC activity and is composed of subscores from endoscopy (range: 0 to 3, where 0 = normal or inactive disease and 3 = severe disease [spontaneous bleeding, ulceration]), rectal bleeding (range: 0 to 3, where 0 = no blood seen and 3 = blood alone passes), stool frequency (range: 0 to 3, where 0 = normal number of stools and 3 = at least 5 or more stools more than normal), and PGA (range: 0 to 3, where 0 = normal and 3 = severe disease). Total score for MCS ranges from 0 to 12 (sum of all subscores), with higher scores indicating higher disease activity. MCS response is defined as a decrease from baseline of ≥ 3 points and at least 30% in MCS, in addition to a ≥ 1 point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore ≤ 1 at Week 10. Participants in the Full Analysis Set were analyzed.

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

End point timeframe:

Week 10

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 7 | 6 | 6 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 28.6 | 16.7 | 16.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved MCS Remission at Week 10

| | |
|-----------------|------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved MCS Remission at Week 10 |
|-----------------|------------------------------------------------------------------|

End point description:

The modified MCS is a scoring system for assessment of UC activity and is composed of subscores from endoscopy (range: 0 to 3, where 0 = normal or inactive disease and 3 = severe disease [spontaneous bleeding, ulceration]), rectal bleeding (range: 0 to 3, where 0 = no blood seen and 3 = blood alone passes), stool frequency (range: 0 to 3, where 0 = normal number of stools and 3 = at least 5 or more stools more than normal), and PGA (range: 0 to 3, where 0 = normal and 3 = severe disease). Total score for MCS ranges from 0 to 12 (sum of all subscores), with higher scores indicating higher disease activity. MCS remission is defined as a MCS score of ≤ 2 and no individual subscore > 1 at Week 10. Participants in the Full Analysis Set were analyzed.

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

End point timeframe:

Week 10

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 7 | 6 | 6 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Histologic Remission Based Upon the Geboes Scale at Week 10

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants Who Achieved Histologic Remission Based Upon the Geboes Scale at Week 10 |
| End point description: | |
| Geboes histologic remission was assessed by the Geboes histologic scores. Grade 0: Architectural changes (0.0=No abnormality to 0.3=Severe diffuse or multifocal abnormalities); Grade 1: Chronic inflammatory infiltrate (1.0=No increase to 1.3=Marked increase); Grade 2A: Eosinophils in lamina propria (2A.0=No increase to 2A.3=Marked increase); Grade 2B: Neutrophils in lamina propria (2B.0=No increase to 2B.3=Marked increase); Grade 3: Neutrophils in epithelium (3.0=None to 3.3=>50% crypts involved); Grade 4: Crypt destruction (4.0=none to 4.3=Unequivocal crypt destruction), and Grade 5: Erosions and ulcerations: (5.0=No erosion, ulceration or granulation to 5.4=Ulcer or granulation tissue). Histologic remission defined as having Grade 0 of ≤ 0.3 , Grade 1 of ≤ 1.1 , Grade 2a of $\leq 2A.3$, Grade 2b of 2B.0, Grade 3 of 3.0, Grade 4 of 4.0, and Grade 5 of 5.0. Score ranges from 0 to 5.4. Lower values indicate better outcome. Participants in the Full Analysis Set with at least 1 histological assessment were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 10 | |

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 6 | 4 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 16.7 | 16.7 | 25.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Treatment-emergent Adverse Events (TEAEs)

| | |
|-----------------|-------------------------------------------------------|
| End point title | Percentage of Participants Who Experienced Treatment- |
|-----------------|-------------------------------------------------------|

End point description:

TEAEs for the Blinded Treatment phase are either defined as AEs with an onset date on or after the Blinded Treatment phase study drug start date and no later than 30 days after permanent discontinuation study drug if no Open-label Treatment phase study drug was taken, or any AEs with an onset date on or after the Blinded Treatment phase study drug start date and before the Open-label Treatment phase study drug start date if Open-label Treatment phase study drug was taken and/or any AEs leading to premature discontinuation of Blinded Treatment phase study drug. TEAEs for the Open-label Treatment phase are either defined as AEs with an onset date on or after the Open-label Treatment phase study drug start date and no later than 30 days after permanent discontinuation of the Open-label Treatment phase study drug and/or any AEs leading to premature discontinuation study drug. Safety Analysis Set included all participants who received at least 1 dose of study drug.

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

End point timeframe:

Blinded Treatment phase: First dose date up to 50.6 weeks plus 30 days; Open-label phase: First dose date up to 50.7 weeks plus 30 days

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | Tilpisertib 300 mg from Tilpisertib 300 mg (OLTP) |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|---------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 4 |
| Units: percentage of participants | | | | |
| number (not applicable) | 57.1 | 50.0 | 50.0 | 50.0 |

| End point values | Tilpisertib 300 mg from Tilpisertib 100 mg (OLTP) | Tilpisertib 300 mg from Placebo (OLTP) | | |
|-----------------------------------|---------------------------------------------------|----------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 3 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 66.7 | 66.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Laboratory Abnormalities

| | |
|-----------------|---------------------------------------------------------------------|
| End point title | Percentage of Participants Who Experienced Laboratory Abnormalities |
|-----------------|---------------------------------------------------------------------|

End point description:

Treatment-emergent laboratory abnormalities for Blinded Treatment phase are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of Blinded Treatment phase study drug plus 30 days for participants who permanently discontinued study drug or before the first dose of Open-label Treatment phase study drug. For the Open-label Treatment phase, treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from Open-label baseline at any postbaseline time point, up to and including the date of last dose of Open-label Treatment phase study drug plus 30 days for participants

who permanently discontinued study drug. For maximum postbaseline toxicity grade, the most severe graded abnormality from all tests was counted for each patient. Grade 1:mild; Grade 2:moderate; Grade 3:severe; Grade 4:life-threatening. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Blinded Treatment phase: First dose date up to 50.6 weeks plus 30 days; Open-label phase: First dose date up to 50.7 weeks plus 30 days

| End point values | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) | Tilpisertib 300 mg from Tilpisertib 300 mg (OLTP) |
|-----------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|---------------------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 4 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Grade 1 | 42.9 | 66.7 | 16.7 | 25.0 |
| Grade 2 | 28.6 | 33.3 | 50.0 | 25.0 |
| Grade 3 | 14.3 | 0 | 0 | 25.0 |
| Grade 4 | 0 | 0 | 0 | 0 |

| End point values | Tilpisertib 300 mg from Tilpisertib 100 mg (OLTP) | Tilpisertib 300 mg from Placebo (OLTP) | | |
|-----------------------------------|---------------------------------------------------|----------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 3 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Grade 1 | 33.3 | 66.7 | | |
| Grade 2 | 0 | 33.3 | | |
| Grade 3 | 66.7 | 0 | | |
| Grade 4 | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Blinded Treatment phase: First dose date up to 50.6 weeks plus 30 days; Open-label Treatment phase: First dose date up to 50.7 weeks plus 30 days; All-Cause Mortality: Enrollment up to Week 70.3

Adverse event reporting additional description:

Adverse Events: Safety Analysis Set included all participants who received at least one 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

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

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------------------------|
| Reporting group title | Tilpisertib 300 mg (Blinded Treatment Phase) |
|-----------------------|----------------------------------------------|

Reporting group description:

Tilpisertib 300 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive tilpisertib 300 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|-----------------------|----------------------------------------------|
| Reporting group title | Tilpisertib 100 mg (Blinded Treatment Phase) |
|-----------------------|----------------------------------------------|

Reporting group description:

Tilpisertib 100 mg tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive tilpisertib 100 mg tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Placebo (Blinded Treatment Phase) |
|-----------------------|-----------------------------------|

Reporting group description:

Placebo tablet orally once daily up to Week 10. Participants who achieved clinical response per modified MCS at Week 10, continued to receive placebo tablets orally once daily for a maximum of 50 weeks in the Blinded Treatment phase.

| | |
|-----------------------|---------------------------------------------------|
| Reporting group title | Tilpisertib 300 mg From Tilpisertib 300 mg (OLTP) |
|-----------------------|---------------------------------------------------|

Reporting group description:

Participants who received tilpisertib 300 mg and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| | |
|-----------------------|---------------------------------------------------|
| Reporting group title | Tilpisertib 300 mg From Tilpisertib 100 mg (OLTP) |
|-----------------------|---------------------------------------------------|

Reporting group description:

Participants who received tilpisertib 100 mg and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| | |
|-----------------------|----------------------------------------|
| Reporting group title | Tilpisertib 300 mg From Placebo (OLTP) |
|-----------------------|----------------------------------------|

Reporting group description:

Participants who received placebo and did not achieve clinical response per modified MCS at Week 10 in the Blinded Treatment phase, received tilpisertib 300 mg tablets orally once daily for up to 50 weeks in the Open-label Treatment phase (OLTP).

| Serious adverse events | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) |
|---------------------------------------------------|----------------------------------------------|----------------------------------------------|-----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |

| | | | |
|-------------------------------------------------|----------------|---------------|----------------|
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Campylobacter infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Tilpisertib 300 mg From Tilpisertib 300 mg (OLTP) | Tilpisertib 300 mg From Tilpisertib 100 mg (OLTP) | Tilpisertib 300 mg From Placebo (OLTP) |
|---------------------------------------------------|------------------------------------------------------|------------------------------------------------------|-------------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Campylobacter infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (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 |

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

| Non-serious adverse events | Tilpisertib 300 mg (Blinded Treatment Phase) | Tilpisertib 100 mg (Blinded Treatment Phase) | Placebo (Blinded Treatment Phase) |
|-------------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 3 / 6 (50.00%) | 2 / 6 (33.33%) |
| General disorders and administration site conditions | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Pulmonary embolism subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 | 1 / 6 (16.67%) 2 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Ear and labyrinth disorders External ear inflammation subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences (all) Dyspepsia | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 6 (0.00%) 0 |
| Haemorrhoids thrombosed subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 2 |
| Rash subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Intervertebral disc protrusion subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Osteonecrosis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Infections and infestations | | | |
| Asymptomatic COVID-19 subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cystitis | | | |

| | | | |
|-----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Mastitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Tilpisertib 300 mg From Tilpisertib 300 mg (OLTP) | Tilpisertib 300 mg From Tilpisertib 100 mg (OLTP) | Tilpisertib 300 mg From Placebo (OLTP) |
|----------------------------------------------------------|---------------------------------------------------------|---------------------------------------------------------|----------------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 2 / 3 (66.67%) |
| General disorders and administration site conditions | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Pulmonary embolism subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Ear and labyrinth disorders External ear inflammation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences (all) Dyspepsia | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |

| | | | |
|------------------------------------------------------------------------------------|---------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Haemorrhoids thrombosed subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Intervertebral disc protrusion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Osteonecrosis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 |
| Infections and infestations | | | |
| Asymptomatic COVID-19 subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Cystitis | | | |

| | | | |
|-----------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mastitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 July 2019 | <ul style="list-style-type: none">- Minor corrections and language revisions were made to provide clarity and consistency throughout the protocol- Updates to the Glossary of Abbreviations and Definition of Terms as needed per revisions to the protocol- Updated Study Design schema (Section 3) to reflect changes made to dosage in the protocol- Updated Study Procedures Table (Appendix 2 and Appendix 3) to reflect changes made to study visits assessments/procedures in the protocol as described in the summary of changes |
| 19 June 2020 | <ul style="list-style-type: none">- Study GS-US-365-4237 is revised to become a blinded study- An unblinded sponsor data review has been added when 90 subjects reach Week 10- Phase 1 study results from GS-US-365-4235 (Phase 1 CYP3A drug-drug interaction study) and GS-US-365-5588 (Phase 1 iohexol study)- Toxicology study results from TX-457-2018 (phototoxicity study in rats) and TX-365-2016 (39-week chronic toxicology study in monkeys)- Revisions to allowed concomitant medications based on the results of Phase 1 Study GS-US-365-4235 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 30 November 2020 | Gilead made the decision to discontinue the development of tilpisertib since a new molecular entity was able to achieve greater target coverage. The decision was not due to any safety concerns. | - |

Notes:

Limitations and caveats

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

Since only 19 participants were enrolled, none of the planned statistical analyses were performed. During the COVID-19 pandemic, there were changes to protocol visits and procedures where necessary to mitigate the impact of the pandemic to the study.

Notes: