



Clinical trial results:

A phase II, randomized, parallel-group, double-blind, placebo-controlled, multicenter study to evaluate the efficacy, safety, and pharmacokinetics of BFKB8488A compared with placebo in patients with non-alcoholic steatohepatitis

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2019-001897-27 |
| Trial protocol | FR BE |
| Global end of trial date | 23 January 2023 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 05 February 2024 |
| First version publication date | 05 February 2024 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GC41033 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04171765 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Hoffmann-La Roche |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, 4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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 February 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 January 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to evaluate the efficacy, safety, and pharmacokinetics of BFKB8488A compared with placebo in participants with non-alcoholic steatohepatitis (NASH).

Protection of trial subjects:

All participants were required to sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 November 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | United States: 45 |
| Worldwide total number of subjects | 46 |
| EEA total number of subjects | 1 |

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) | 37 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult participants (ages 18-75 inclusive) with non-alcoholic steatohepatitis as confirmed through central testing of a representative liver sample.

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 | Placebo |

Arm description:

Participants received placebo by subcutaneous (SC) injection every two weeks (Q2W) for 52 weeks.

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

Dosage and administration details:

Given subcutaneously every two weeks for 52 weeks.

| | |
|------------------|------------------|
| Arm title | Fixed Dose 50 mg |
|------------------|------------------|

Arm description:

Participants received 50 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fazpilodemab |
| Investigational medicinal product code | |
| Other name | BFKB8488A |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Given subcutaneously every two weeks for 52 weeks.

| | |
|------------------|------------------|
| Arm title | Fixed Dose 75 mg |
|------------------|------------------|

Arm description:

Participants received 75 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fazpilodemab |
| Investigational medicinal product code | |
| Other name | BFKB8488A |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Given subcutaneously every two weeks for 52 weeks.

| | |
|---|------------------------|
| Arm title | Fixed Dose 100 mg |
| Arm description: | |
| Participants received 100 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Fazpilodemab |
| Investigational medicinal product code | |
| Other name | BFKB8488A |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Given subcutaneously every two weeks for 52 weeks.

| Number of subjects in period 1 | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg |
|---------------------------------------|---------|------------------|------------------|
| Started | 13 | 11 | 11 |
| Completed | 8 | 9 | 7 |
| Not completed | 5 | 2 | 4 |
| Consent withdrawn by subject | 1 | - | - |
| Adverse event, non-fatal | 2 | - | 1 |
| Week 58 visit missed | - | - | 1 |
| Study terminated by sponsor | 2 | - | - |
| Lost to follow-up | - | 2 | 2 |

| Number of subjects in period 1 | Fixed Dose 100 mg |
|---------------------------------------|-------------------|
| Started | 11 |
| Completed | 6 |
| Not completed | 5 |
| Consent withdrawn by subject | 3 |
| Adverse event, non-fatal | - |
| Week 58 visit missed | - |
| Study terminated by sponsor | - |
| Lost to follow-up | 2 |

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo by subcutaneous (SC) injection every two weeks (Q2W) for 52 weeks. | |
| Reporting group title | Fixed Dose 50 mg |
| Reporting group description: | |
| Participants received 50 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks. | |
| Reporting group title | Fixed Dose 75 mg |
| Reporting group description: | |
| Participants received 75 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks. | |
| Reporting group title | Fixed Dose 100 mg |
| Reporting group description: | |
| Participants received 100 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks. | |

| Reporting group values | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg |
|---|---------|------------------|------------------|
| Number of subjects | 13 | 11 | 11 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 12 | 8 | 9 |
| From 65-84 years | 1 | 3 | 2 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 48.4 | 57.4 | 55.4 |
| standard deviation | ± 9.6 | ± 10.0 | ± 8.2 |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 6 | 6 | 6 |
| Male | 7 | 5 | 5 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 1 |
| White | 13 | 10 | 9 |
| More than one race | 0 | 0 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 7 | 5 | 3 |
| Not Hispanic or Latino | 6 | 6 | 8 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | Fixed Dose 100 mg | Total | |
|------------------------|-------------------|-------|--|
| Number of subjects | 11 | 46 | |

| | | | |
|---|--------|----|--|
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 8 | 37 | |
| From 65-84 years | 3 | 9 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 51.9 | | |
| standard deviation | ± 14.8 | - | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 6 | 24 | |
| Male | 5 | 22 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 1 | 1 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 2 | |
| White | 10 | 42 | |
| More than one race | 0 | 1 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 5 | 20 | |
| Not Hispanic or Latino | 6 | 26 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo by subcutaneous (SC) injection every two weeks (Q2W) for 52 weeks. | |
| Reporting group title | Fixed Dose 50 mg |
| Reporting group description: | |
| Participants received 50 mg of SC fapzilodemab (BFKB8488A) Q2W for 52 weeks. | |
| Reporting group title | Fixed Dose 75 mg |
| Reporting group description: | |
| Participants received 75 mg of SC fapzilodemab (BFKB8488A) Q2W for 52 weeks. | |
| Reporting group title | Fixed Dose 100 mg |
| Reporting group description: | |
| Participants received 100 mg of SC fapzilodemab (BFKB8488A) Q2W for 52 weeks. | |

Primary: Proportion of Participants with NASH Resolution on Overall Histopathological Reading Without Worsening of Fibrosis at Week 52

| | |
|--|--|
| End point title | Proportion of Participants with NASH Resolution on Overall Histopathological Reading Without Worsening of Fibrosis at Week 52 ^[1] |
| End point description: | |
| Resolution of non-alcoholic steatohepatitis (NASH) is defined as a non-alcoholic fatty liver disease activity score (NAS) of 0–1 for inflammation, 0 for ballooning, and any value for steatosis as determined by a central reader. Worsening of fibrosis is defined as any increase in NASH Clinical Research Network (CRN) fibrosis stage as determined by a central reader. | |
| End point type | Primary |
| End point timeframe: | |
| Week 52 | |

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 analysis was planned for this endpoint.

| End point values | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg | Fixed Dose 100 mg |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 8 | 7 | 6 |
| Units: Proportion of Participants | | | | |
| number (confidence interval 95%) | 16.7 (0.00 to 54.82) | 37.5 (0.00 to 77.30) | 14.3 (0.00 to 47.35) | 33.3 (0.00 to 79.39) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hepatic Fat Fraction as Assessed by Magnetic Resonance Imaging-Derived Proton Density Fat Fraction (MRI-PDFF) at Week 52

| | |
|-----------------|---|
| End point title | Change from Baseline in Hepatic Fat Fraction as Assessed by |
|-----------------|---|

End point description:

End point type Secondary

End point timeframe:

Baseline, Week 16, Week 52

| End point values | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg | Fixed Dose 100 mg |
|--------------------------------------|-----------------|------------------|------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 11 | 11 | 11 |
| Units: No units | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 20.15 (± 6.35) | 20.67 (± 6.05) | 19.30 (± 3.99) | 18.12 (± 7.70) |
| Week 16 change from baseline | -3.47 (± 2.28) | -8.20 (± 8.58) | -2.23 (± 9.05) | -10.25 (± 4.76) |
| Week 52 change from baseline | -4.46 (± 6.23) | -2.50 (± 8.13) | -3.46 (± 11.57) | -3.53 (± 6.54) |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with Improvement in Liver Histology from Baseline and no Worsening of Fibrosis at Week 52

End point title Proportion of Participants with Improvement in Liver Histology from Baseline and no Worsening of Fibrosis at Week 52

End point description:

End point type Secondary

End point timeframe:

Week 52

| End point values | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg | Fixed Dose 100 mg |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 8 | 7 | 6 |
| Units: Proportion of participants | | | | |
| number (confidence interval 95%) | 16.7 (0.00 to 54.82) | 37.5 (0.00 to 77.30) | 42.9 (0.00 to 86.66) | 33.3 (0.00 to 79.39) |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with Improvement in Liver Fibrosis of at Least One Stage, as Defined by NASH Clinical Research Network (CRN), and no Worsening of NASH at Week 52

| | |
|-----------------|--|
| End point title | Proportion of Participants with Improvement in Liver Fibrosis of at Least One Stage, as Defined by NASH Clinical Research Network (CRN), and no Worsening of NASH at Week 52 |
|-----------------|--|

End point description:

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

End point timeframe:

Week 52

| End point values | Placebo | Fixed Dose 50 mg | Fixed Dose 75 mg | Fixed Dose 100 mg |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 8 | 7 | 6 |
| Units: Proportion of participants | | | | |
| number (confidence interval 95%) | 16.7 (0.00 to 54.82) | 25.0 (0.00 to 61.26) | 28.6 (0.00 to 69.18) | 16.7 (0.00 to 54.82) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through Week 58

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received placebo by subcutaneous (SC) injection every two weeks (Q2W) for 52 weeks.

| | |
|-----------------------|---------------------------|
| Reporting group title | Fixed Dose-75mg BFKB8488A |
|-----------------------|---------------------------|

Reporting group description:

Participants received 75 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks.

| | |
|-----------------------|----------------------------|
| Reporting group title | Fixed Dose-100mg BFKB8488A |
|-----------------------|----------------------------|

Reporting group description:

Participants received 100 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks.

| | |
|-----------------------|---------------------------|
| Reporting group title | Fixed Dose-50mg BFKB8488A |
|-----------------------|---------------------------|

Reporting group description:

Participants received 50 mg of SC fazpilodemab (BFKB8488A) Q2W for 52 weeks.

| Serious adverse events | Placebo | Fixed Dose-75mg BFKB8488A | Fixed Dose-100mg BFKB8488A |
|---|----------------|------------------------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (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

| | | |
|------------------------------|--|--|
| Fixed Dose-50mg BFKB8488A | | |
|------------------------------|--|--|

| | | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| 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 | Placebo | Fixed Dose-75mg BFKB8488A | Fixed Dose-100mg BFKB8488A |
|---|-----------------|------------------------------|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 13 (69.23%) | 9 / 11 (81.82%) | 10 / 11 (90.91%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign neoplasm of thyroid gland | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|------------------------------|-----------------|----------------|-----------------|
| Administration site pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Administration site swelling | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 4 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 0 | 2 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 2 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site urticaria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| Pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Vaccination site pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast calcifications | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Breast tenderness | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vaginal discharge | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal septum deviation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nasal valve collapse | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Respiratory disorder subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Emotional disorder subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Blood iron decreased subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Blood pressure increased subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Cortisol free urine increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Insulin-like growth factor decreased | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth fracture | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Carpal tunnel syndrome | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Neuralgia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 11 (27.27%) | 4 / 11 (36.36%) |
| occurrences (all) | 0 | 4 | 4 |
| Abdominal pain upper | | | |

| | | | |
|----------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 1 | 3 |
| Colitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenal polyp | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 2 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 1 / 11 (9.09%) | 5 / 11 (45.45%) |
| occurrences (all) | 3 | 1 | 12 |
| Vomiting | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 3 | 2 / 11 (18.18%) 2 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 3 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---------------------------------|-----------------|-----------------|-----------------|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 2 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 11 (27.27%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 3 | 2 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 0 | 2 |
| Sacral pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 11 (9.09%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 1 | 2 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |

| | | | |
|------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 11 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 11 (0.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 0 | 0 | 4 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 11 (9.09%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Gout subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 |
| Increased appetite subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 1 / 11 (9.09%) 1 |
| Vitamin D deficiency subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 11 (9.09%) 1 | 1 / 11 (9.09%) 1 |

| | | | |
|--|------------------------------|--|--|
| Non-serious adverse events | Fixed Dose-50mg BFBK8488A | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 11 / 11 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign neoplasm of thyroid gland subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | | |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | | |
| Hypertension subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | | |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | | |

| | | | |
|--|----------------|--|--|
| General disorders and administration site conditions | | | |
| Administration site pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Administration site swelling | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Early satiety | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Injection site pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 3 | | |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site urticaria | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vaccination site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> | | |
| <p>Reproductive system and breast disorders</p> <p>Breast calcifications</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Breast tenderness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Postmenopausal haemorrhage</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pelvic pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vaginal discharge</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Nasal septum deviation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal valve collapse</p> | <p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p> | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | | |
| occurrences (all) | 2 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Emotional disorder | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood pressure increased | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cortisol free urine increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Insulin-like growth factor decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |

| | | | |
|-----------------------------|----------------|--|--|
| Dizziness | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Retinal tear | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 3 / 11 (27.27%) | | |
| occurrences (all) | 5 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Colitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 2 | | |
| Duodenal polyp | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 3 | | |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 3 / 11 (27.27%) | | |
| occurrences (all) | 5 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | | |
| occurrences (all) | 2 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Night sweats | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pollakiuria | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sacral pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 5 / 11 (45.45%) | | |
| occurrences (all) | 5 | | |
| Herpes zoster | | | |

| | | | |
|------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | | |
| occurrences (all) | 2 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Gout | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 1 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |
| Increased appetite | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | | |
| occurrences (all) | 2 | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 23 August 2019 | The exclusion criteria were updated to exclude patients with various additional endocrine, hepatic, and skeletal pathologies in consideration of overall patient safety and the potential risks of fazpilodemab. Additionally, the current or prior use of selected medications impacting hypothalamic-pituitary-adrenal (HPA) axis and bone mineral density was added as exclusion criteria. |
| 09 March 2020 | The use of glucocorticoids was further clarified to exclude systemic glucocorticoids. The use of glucagon-like peptide-1 (GLP-1) receptor agonists was amended to allow patients who were treated with a stable dose of GLP-1 for at least 6 months prior to the qualifying liver biopsy. The exclusion criterion for patients with cholelithiasis was removed. The exclusion criterion for patients with vitamin D deficiency (< 20 ng/mL) was amended because the majority of patients with metabolic syndrome and/or NASH are vitamin D insufficient. |
| 28 October 2020 | The exclusion criterion for drugs prolonging QT was removed. The exclusion criterion for drugs historically associated with NAFLD was further clarified as the intent of the criterion was to exclude drugs that might cause steatohepatitis. The hepatitis B virus (HBV) exclusion criterion was updated to clarify that the HBV DNA was a reflexive laboratory test that should be done to confirm past or resolved HBV infection in patients with the presence of hepatitis B core antibody and absence of hepatitis B surface antigen. The HBV and hepatitis C reflex laboratory tests were further clarified. The PHQ-9 exclusion criterion was updated to more accurately identify patients at higher risk for self-harm including suicidal ideation or behavior. |
| 12 January 2021 | The initial screen FibroScan(TM) inclusion criteria for potential participants who do not have a qualifying historical liver biopsy were modified. The study design was clarified to separate the conduct of the fixed dosing cohort and the individualized dosing cohort. Vaccines against the SARS-CoV-2 virus were added to the permitted medications. The thyroid exclusion criteria as well as permitted and prohibited thyroid therapies were revised to clarify the screening testing and hypo- and hyperthyroid treatment requirements. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Because the study was terminated early, the interpretation of its data is limited, and early dropout may confound the results.

Notes: