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 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.	

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

	Magnetic Resonance Imaging-Derived Proton Density Fat Fraction (MRI-PDFF) at Week 52

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	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Emotional disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Blood cholesterol increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	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	1 / 13 (7.69%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	1	3	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	0 / 13 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Increased appetite			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Vitamin D deficiency			
subjects affected / exposed	1 / 13 (7.69%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	1	1	1

Non-serious adverse events	Fixed Dose-50mg BFKB8488A		
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	0 / 11 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	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			

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

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 occurrences (all)	1 / 11 (9.09%) 1		
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Neuralgia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Tremor subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Retinal tear subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 4		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 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 occurrences (all)	3 / 11 (27.27%) 5		
Vomiting subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Night sweats subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Urticaria subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 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 occurrences (all)	0 / 11 (0.00%) 0		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Gout subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Increased appetite subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2		
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 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: