



Clinical trial results:

A Multicentre, Randomized, Double Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GFT505 once daily on Steatohepatitis in Patients with Non-Alcoholic Steatohepatitis (NASH).

Summary

EudraCT number	2012-000295-42
Trial protocol	BE DE ES GB NL IT
Global end of trial date	27 February 2015

Results information

Result version number	v2 (current)
This version publication date	29 January 2023
First version publication date	12 May 2022
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Corrected following updates to clinicaltrials.gov

Trial information

Trial identification

Sponsor protocol code	GFT505-212-7
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01694849
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GENFIT
Sponsor organisation address	Parc Eurasanté, 885, avenue Eugène Avinée, Loos, France, 59120
Public contact	Genfit, Genfit, +33 3 20 16 40 00, clinicaltrial@genfit.com
Scientific contact	Carol Addy, MD MSc, Genfit, +33 6179536469,

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	28 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GFT505 80mg and GFT505 120mg once daily for 52 weeks versus placebo in reversing histological steatohepatitis without worsening of fibrosis.

Worsening of fibrosis is evaluated using NASH CRN fibrosis staging system and defined as:

- Progression to stage 3 or 4 for patients at stage 0, 1 or 2 on diagnostic liver biopsy,
- Progression to stage 4 for patients at stage 3 on diagnostic liver biopsy.

Protection of trial subjects:

Continuing safety of trial participants in this Phase IIB study was ensured through regular safety reviews and DSMB analyses.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Belgium: 37
Country: Number of subjects enrolled	France: 69
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	United States: 108
Worldwide total number of subjects	274
EEA total number of subjects	166

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)	240
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment for the GFT505-212-7 study began in September 2012. This was a phase IIb, double-blind, randomized, placebo-controlled study conducted in three parallel groups: placebo, GFT505 80mg and GFT505 120mg (after DSMB review of 6 month safety data of the 80mg dose on at least 50% of participants) once daily for 52 weeks.

Pre-assignment

Screening details:

Random allocation was done in two phases. First phase, participants were randomly allocated to GFT505 80 mg or placebo (ratio 2:1). Second phase (after DSMB review of 6-month safety data of 80-mg dose on $\geq 50\%$ of participants), participants were assigned to GFT505 120 mg or placebo (ratio 2:1) in order to balance the 3 treatments in 1:1:1 ratio.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The Investigator, patient, and study personnel were blinded to the treatment. Identification's number were assigned to a patient at the selection visit. Upon completion of the baseline visit(s), eligible patients were randomly assigned to active treatment (GFT505 80mg or GFT505 120mg or placebo).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	GFT505 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

3 capsules of placebo / day

Arm title	GFT505 120mg
------------------	--------------

Arm description:

90 subjects were randomised to GFT505 120mg arm but one subject was not treated, and is not counted in this arm.

This subject is excluded from the baseline characteristics reporting and the safety data analysis population

Arm type	Experimental
Investigational medicinal product name	GFT505 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GFT505 120mg arm: 3 capsules of GFT505 40 mg / day

Arm title	GFT505 80mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GFT505 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
GFT505 80mg arm: 3 capsules / day : 2 capsules of GFT505 40 mg and 1 capsule of placebo	
Investigational medicinal product name	GFT505 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
GFT505 80mg arm: 3 capsules / day : 2 capsules of GFT505 40 mg and 1 capsule of placebo	

Number of subjects in period 1	Placebo	GFT505 120mg	GFT505 80mg
Started	92	89	93
Completed	78	79	84
Not completed	14	10	9
Consent withdrawn by subject	7	3	1
Adverse event, non-fatal	4	7	6
Non-compliance	1	-	1
Protocol specific withdrawal criterion	1	-	1
Lost to follow-up	1	-	-

Period 2	
Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	GFT505 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
3 capsules of placebo / day	
Arm title	GFT505 120mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GFT505 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
GFT505 120mg arm: 3 capsules of GFT505 40 mg / day	
Arm title	GFT505 80mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GFT505 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
GFT505 80mg arm: 3 capsules / day : 2 capsules of GFT505 40 mg and 1 capsule of placebo	
Investigational medicinal product name	GFT505 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
GFT505 80mg arm: 3 capsules / day : 2 capsules of GFT505 40 mg and 1 capsule of placebo	

Number of subjects in period 2	Placebo	GFT505 120mg	GFT505 80mg
Started	78	79	84
Completed	77	76	83
Not completed	1	3	1
Consent withdrawn by subject	-	1	-
Lost to follow-up	1	2	1

Baseline characteristics

Reporting groups

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

Reporting group description: -

Reporting group title	GFT505 120mg
-----------------------	--------------

Reporting group description:

90 subjects were randomised to GFT505 120mg arm but one subject was not treated, and is not counted in this arm.

This subject is excluded from the baseline characteristics reporting and the safety data analysis population

Reporting group title	GFT505 80mg
-----------------------	-------------

Reporting group description: -

Reporting group values	Placebo	GFT505 120mg	GFT505 80mg
Number of subjects	92	89	93
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	52.88	52.88	53.26
standard deviation	± 11.99	± 11.63	± 11.02
Gender categorical Units: Subjects			
Female	37	42	44
Male	55	47	49
Race Units: Subjects			
Caucasian	85	71	88
Black	3	5	2
Asian	1	6	0
Other	3	7	3
Prevalence of type 2 diabetes mellitus Units: Subjects			
Type 2 diabetes- Yes	33	37	37
Type 2 diabetes- No	59	52	56

Body Mass Index Units: kilogram(s)/square meter arithmetic mean standard deviation	30.91 ± 4.15	31.04 ± 4.39	31.80 ± 5.20
Waist circumference Units: centimeter arithmetic mean standard deviation	104.68 ± 10.52	106.26 ± 10.28	106.41 ± 13.09
Height Units: cm arithmetic mean standard deviation	169.21 ± 10.23	170.21 ± 10.69	167.77 ± 9.30
Weight Units: kg arithmetic mean standard deviation	88.72 ± 15.79	90.15 ± 15.57	88.72 ± 15.79

Reporting group values	Total		
Number of subjects	274		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	123		
Male	151		
Race Units: Subjects			
Caucasian	244		
Black	10		
Asian	7		
Other	13		
Prevalence of type 2 diabetes mellitus Units: Subjects			
Type 2 diabetes- Yes	107		
Type 2 diabetes- No	167		

Body Mass Index Units: kilogram(s)/square meter arithmetic mean standard deviation	-		
Waist circumference Units: centimeter arithmetic mean standard deviation	-		
Height Units: cm arithmetic mean standard deviation	-		
Weight Units: kg arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	GFT505 120mg
Reporting group description: 90 subjects were randomised to GFT505 120mg arm but one subject was not treated, and is not counted in this arm. This subject is excluded from the baseline characteristics reporting and the safety data analysis population	
Reporting group title	GFT505 80mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	GFT505 120mg
Reporting group description: -	
Reporting group title	GFT505 80mg
Reporting group description: -	
Subject analysis set title	EES (ITT)- Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT population or Efficacy Evaluable Set (EES) included all randomised and treated patients with a liver biopsy at endpoint.	
Subject analysis set title	EES (ITT)- GFT505 80mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT population or Efficacy Evaluable Set (EES) included all randomised and treated patients with a liver biopsy at endpoint.	
Subject analysis set title	EES (ITT)- GFT505 120mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT population or Efficacy Evaluable Set (EES) included all randomised and treated patients with a liver biopsy at endpoint.	

Primary: EES- Percentage of Responders With Disappearance of Steatohepatitis Without Worsening of Fibrosis (ie, Participants no Longer Meeting the Criteria for Steatohepatitis)

End point title	EES- Percentage of Responders With Disappearance of Steatohepatitis Without Worsening of Fibrosis (ie, Participants no Longer Meeting the Criteria for Steatohepatitis)
End point description: The primary endpoint was the percentage of responders at W52, defined by the disappearance of steatohepatitis (i.e. patients no longer meeting the criteria for steatohepatitis) without worsening of fibrosis (worsening of fibrosis was evaluated using NASH CRN fibrosis staging system and was defined as progression to stage 3 or 4 for patients at stage 0, 1 or 2 on diagnostic liver biopsy or progression to stage 4 for patients at stage 3 on diagnostic liver biopsy.	
End point type	Primary
End point timeframe: Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: percent				
number (not applicable)	20.8	25.6	24.4	

Statistical analyses

Statistical analysis title	EES (ITT) GFT505 120mg vs Placebo
Statistical analysis description: H_01: OR_80 less than or equal to 1 versus H_11 : OR_80 greater than 1 H_02: OR_120 less than or equal to 1 versus H_12 : OR_120 greater than 1	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.816 ^[2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.897
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.361
upper limit	2.232
Variability estimate	Standard error of the mean

Notes:

[1] - Baseline NAS, Log transformed baseline aspartate aminotransferase and baseline plasminogen activator inhibitor 1 values

[2] - To deal with multiplicity of comparisons, a step-down approach was adopted to control the type I error to 0.05. The contrast GFT120 mg versus placebo was examined first. If not significant the GFT 80mg versus placebo contrast was not examined.

Statistical analysis title	EES (ITT) GFT505 80mg vs Placebo
Statistical analysis description: H_01: OR_80 less than or equal to 1 versus H_11 : OR_80 greater than 1 H_02: OR_120 less than or equal to 1 versus H_12 : OR_120 greater than 1	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.8539 ^[4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.427
upper limit	2.795

Variability estimate	Standard error of the mean
----------------------	----------------------------

Notes:

[3] - Baseline NAS, Log transformed baseline aspartate aminotransferase and baseline plasminogen activator inhibitor 1 values

[4] - To deal with multiplicity of comparisons, a step-down approach was adopted to control the type I error to 0.05. The contrast GFT120 mg versus placebo was examined first. If not significant the GFT 80mg versus placebo contrast was not examined.

Secondary: EES- Change From Baseline to Week 52 in Non-alcoholic Fatty Liver Disease Activity Score

End point title	EES- Change From Baseline to Week 52 in Non-alcoholic Fatty Liver Disease Activity Score
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg the change from baseline to Week 52, in Non-alcoholic Fatty Liver Disease Activity Score (NAS score).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: NAS score delta				
arithmetic mean (standard deviation)	-0.45 (± 1.34)	-0.65 (± 1.33)	-0.64 (± 1.68)	

Statistical analyses

Statistical analysis title	Difference in LS mean 80mg vs placebo
----------------------------	---------------------------------------

Statistical analysis description:

H0: difference in least squares (LS) mean change from baseline equal to 0 H1: difference in LS mean change from baseline not equal to 0

Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.225 ^[5]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.2
Variability estimate	Standard error of the mean

Notes:

[5] - Baseline Non-Alcoholic Fatty Liver Disease Activity Score

Statistical analysis title	Difference in LS mean 120mg vs placebo
Statistical analysis description: H0: difference in least squares (LS) mean change from baseline equal to 0 H1: difference in LS mean change from baseline not equal to 0 Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.254 ^[6]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.2
Variability estimate	Standard error of the mean

Notes:

[6] - Baseline Non-Alcoholic Fatty Liver Disease Activity Score

Secondary: EES- Number of Participants With Decrease in Steatosis Score of at Least 1 Point Between Baseline and Week 52

End point title	EES- Number of Participants With Decrease in Steatosis Score of at Least 1 Point Between Baseline and Week 52
End point description: To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, number of participants with a decrease in steatosis score of at least 1 point between baseline and Week 52	
End point type	Secondary
End point timeframe: Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77 ^[7]	82 ^[8]	78 ^[9]	
Units: number of subjects				
number (not applicable)				
Mild (NFLDA score 3)	0	1	1	
Moderate (NFLDA score 4-5)	12	13	10	
Severe (NFLDA score 6-8)	3	3	10	
Total	15	17	21	

Notes:

[7] - Mild 14 subjects analysed, Moderate 41 subjects analysed, Severe 22 subjects analysed.

[8] - Mild 10 subjects analysed, Moderate 49 subjects analysed, Severe 23 subjects analysed.

[9] - Mild 11 subjects analysed, Moderate 40 subjects analysed, Severe 27 subjects analysed.

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5231 ^[10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.723
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.267
upper limit	1.958
Variability estimate	Standard error of the mean

Notes:

[10] - Baseline value of the analyzed parameter

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8459 ^[11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.102
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.415
upper limit	2.924
Variability estimate	Standard error of the mean

Notes:

[11] - Baseline value of the analyzed parameter

Secondary: EES- Number of Participants With Decrease in Lobular Inflammation Score of at Least 1 Point Between Baseline and Week 52

End point title	EES- Number of Participants With Decrease in Lobular Inflammation Score of at Least 1 Point Between Baseline and Week 52
End point description: To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, number of participants with a decrease in lobular inflammation score of at least 1 point between baseline and Week 52	
End point type	Secondary
End point timeframe: Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77 ^[12]	82 ^[13]	78 ^[14]	
Units: number of subjects				
number (not applicable)				
Mild (NFLDA score 3)	7	1	2	
Moderate (NFLDA score 4-5)	8	10	11	
Severe (NFLDA score 6-8)	12	14	16	
Total	27	25	29	

Notes:

[12] - Mild 14 subjects analysed, Moderate 41 subjects analysed, Severe 22 subjects analysed.

[13] - Mild 10 subjects analysed, Moderate 49 subjects analysed, Severe 23 subjects analysed.

[14] - Mild 11 subjects analysed, Moderate 40 subjects analysed, Severe 27 subjects analysed.

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Statistical analysis description: Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5229 ^[15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.638
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.161
upper limit	2.529
Variability estimate	Standard error of the mean

Notes:

[15] - Baseline value of the analyzed parameter

Statistical analysis title	GFT505 120mg, Placebo
-----------------------------------	-----------------------

Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5646 ^[16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.433
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.421
upper limit	4.875
Variability estimate	Standard error of the mean

Notes:

[16] - Baseline value of the analyzed parameter

Secondary: EES - Decrease in Ballooning Score of at Least 1 Point Between Baseline and Week 52

End point title	EES - Decrease in Ballooning Score of at Least 1 Point Between Baseline and Week 52
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, number of participants with a decrease in ballooning score of at least 1 point between baseline and Week 52

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: percent				
number (not applicable)	31.17	37.80	38.46	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
----------------------------	----------------------

Statistical analysis description:

Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
-------------------	---

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1983 ^[17]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.382
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.088
upper limit	1.656
Variability estimate	Standard error of the mean

Notes:

[17] - Baseline value of the analyzed parameter

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1 ^[18]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.268
upper limit	3.466
Variability estimate	Standard error of the mean

Notes:

[18] - Baseline value of the analyzed parameter

Secondary: EES - Changes From Baseline to Week 52 in the Stages of Fibrosis

End point title	EES - Changes From Baseline to Week 52 in the Stages of Fibrosis
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in stages of fibrosis (based on Non-Alcoholic Steatohepatitis Clinical Research Network [NASH CRN] scoring).	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: change in fibrosis score				
arithmetic mean (standard deviation)	-0.23 (± 0.90)	-0.23 (± 0.84)	-0.06 (± 0.96)	

Statistical analyses

Statistical analysis title	GFT505 80mg, vsPlacebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3543
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.653
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.265
upper limit	1.609
Variability estimate	Standard error of the mean

Statistical analysis title	GFT505 120mg vs Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.578
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.547
upper limit	2.953
Variability estimate	Standard error of the mean

Secondary: EES - Changes From Baseline to Visit 8 (Week 52) in Gamma-glutamyl transferase (GGT)

End point title	EES - Changes From Baseline to Visit 8 (Week 52) in Gamma-glutamyl transferase (GGT)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in liver enzymes.

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: U/L				
arithmetic mean (standard deviation)	6.22 (\pm 50.64)	-24.32 (\pm 36.39)	-20.59 (\pm 40.45)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
-----------------------------------	----------------------

Statistical analysis description:

Change in Gamma-glutamyl transferase (U/L)

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
-------------------	---

Number of subjects included in analysis	159
---	-----

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	superiority
---------------	-------------

P-value	< 0.001
---------	---------

Method	Mixed models analysis
--------	-----------------------

Parameter estimate	difference in least square mean change
--------------------	--

Point estimate	-31.41
----------------	--------

Confidence interval

level	95 %
-------	------

sides	2-sided
-------	---------

lower limit	-43.78
-------------	--------

upper limit	-19.15
-------------	--------

Variability estimate	Standard error of the mean
----------------------	----------------------------

Statistical analysis title	GFT505 120mg, Placebo
-----------------------------------	-----------------------

Statistical analysis description:

Change in Gamma-glutamyl transferase (U/L)

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
-------------------	--

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-29.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.84
upper limit	-16.77
Variability estimate	Standard error of the mean

Secondary: EES- Changes From Baseline to Visit 8 (Week 52) in Aspartate Transaminase/Alanine Aminotransferase Ratio

End point title	EES- Changes From Baseline to Visit 8 (Week 52) in Aspartate Transaminase/Alanine Aminotransferase Ratio
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in aspartate transaminase/alanine aminotransferase ratio.	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: AST/ALT delta				
arithmetic mean (standard deviation)	0.01 (± 0.25)	0.15 (± 0.21)	0.20 (± 0.25)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[19]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.21
Variability estimate	Standard error of the mean

Notes:

[19] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[20]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.26
Variability estimate	Standard error of the mean

Notes:

[20] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES- Change From Baseline to Week 52 in Non-alcoholic Fatty Liver Disease Activity Score of at least 2 points.

End point title	EES- Change From Baseline to Week 52 in Non-alcoholic Fatty Liver Disease Activity Score of at least 2 points.
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg the change from baseline to Week 52, in Non-alcoholic Fatty Liver Disease Activity Score (NAS score) of at least 2 points.

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: percent				
number (not applicable)	27.27	25.61	33.33	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority ^[21]
P-value	= 0.8586 ^[22]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.073
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.493
upper limit	2.339
Variability estimate	Standard error of the mean

Notes:

[21] - To take into account the inflation of type I error due to multiple comparisons without changing the nominal type I error risk, a step-down approach was adopted. .The first contrast to be examined was the contrast GFT120 mg versus placebo. If not significant the GFT 80mg versus placebo contrast was not examined. Therefore the type I error risk was set at 0.05

[22] - Baseline Non-Alcoholic Fatty Liver Disease Activity Score

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description:	
Population with baseline Non-Alcoholic Fatty Liver Disease Activity Score greater than or equal to 4	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority ^[23]
P-value	= 0.2255 ^[24]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.601
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.747
upper limit	2.432
Variability estimate	Standard error of the mean

Notes:

[23] - To take into account the inflation of type I error due to multiple comparisons without changing the nominal type I error risk, a step-down approach was adopted. .The first contrast to be examined was the contrast GFT120 mg versus placebo. If not significant the GFT 80mg versus placebo contrast was not examined. Therefore the type I error risk was set at 0.05

[24] - Baseline Non-Alcoholic Fatty Liver Disease Activity Score

Secondary: EES - Changes From Baseline to Visit 8 (Week 52) in alkaline phosphatases

End point title	EES - Changes From Baseline to Visit 8 (Week 52) in alkaline phosphatases
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from

baseline to
week 52, in liver enzymes.

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: U/L				
arithmetic mean (standard deviation)	3.44 (± 13.16)	-18.82 (± 13.23)	-20.44 (± 16.47)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
-----------------------------------	----------------------

Statistical analysis description:

Change in Alkaline phosphatases (U/L)

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[25]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-23.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.16
upper limit	-18.88
Variability estimate	Standard error of the mean

Notes:

[25] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
-----------------------------------	-----------------------

Statistical analysis description:

Change in Alkaline phosphatases (U/L)

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[26]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-23.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.04
upper limit	2.12
Variability estimate	Standard error of the mean

Notes:

[26] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in triglycerides

End point title	EES - Changes From Baseline to Week 52 in triglycerides
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.16 (± 1.12)	-0.33 (± 0.76)	-0.48 (± 0.90)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[27]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.21
Variability estimate	Standard error of the mean

Notes:

[27] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
-----------------------------------	-----------------------

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[28]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.29
Variability estimate	Standard error of the mean

Notes:

[28] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in cholesterol

End point title	EES - Changes From Baseline to Week 52 in cholesterol
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.02 (± 0.66)	-0.42 (± 0.78)	-0.42 (± 0.72)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 ^[29]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.35

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	-0.14
Variability estimate	Standard error of the mean

Notes:

[29] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[30]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.43

Confidence interval

level	95 %
sides	2-sided
lower limit	-0.64
upper limit	-0.23
Variability estimate	Standard error of the mean

Notes:

[30] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Change in Non-high Density Lipoproteins Cholesterol (nHDL-c)

End point title	EES - Change in Non-high Density Lipoproteins Cholesterol (nHDL-c)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.07 (± 0.67)	-0.45 (± 0.79)	-0.47 (± 0.71)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[31]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	-0.24
Variability estimate	Standard error of the mean

Notes:

[31] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[32]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.32
Variability estimate	Standard error of the mean

Notes:

[32] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Change in High Density Lipoproteins Cholesterol (HDL-c)

End point title	EES - Change in High Density Lipoproteins Cholesterol (HDL-c)
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.06 (± 0.21)	0.02 (± 0.17)	0.06 (± 0.23)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 ^[33]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.15
Variability estimate	Standard error of the mean

Notes:

[33] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[34]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.17
Variability estimate	Standard error of the mean

Notes:

[34] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Change in Very Low Density Lipoproteins Cholesterol (VLDL-c)

End point title	EES - Change in Very Low Density Lipoproteins Cholesterol (VLDL-c)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	75	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.05 (± 0.23)	-0.17 (± 0.28)	-0.17 (± 0.32)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[35]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.11
Variability estimate	Standard error of the mean

Notes:

[35] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[36]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	-0.09
Variability estimate	Standard error of the mean

Notes:

[36] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES- Change in Low Density Lipoproteins Cholesterol (LDL-c)

End point title	EES- Change in Low Density Lipoproteins Cholesterol (LDL-c)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in lipid parameters (used to assess cardiovascular risk)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	75	
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.01 (± 0.51)	-0.27 (± 0.70)	-0.25 (± 0.61)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 ^[37]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	-0.02
Variability estimate	Standard error of the mean

Notes:

[37] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
-----------------------------------	-----------------------

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 ^[38]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.06
Variability estimate	Standard error of the mean

Notes:

[38] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Visit 8 (Week 52) in Aspartate Transaminase (AST)

End point title	EES - Changes From Baseline to Visit 8 (Week 52) in Aspartate Transaminase (AST)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in liver enzymes.

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: U/L				
arithmetic mean (standard deviation)	-1.32 (± 16.63)	1.88 (± 27.76)	-1.37 (± 24.74)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
-----------------------------------	----------------------

Statistical analysis description:

Change in aspartate transaminase (U/L)

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
-------------------	---

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711 ^[39]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.33
upper limit	7.81
Variability estimate	Standard error of the mean

Notes:

[39] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description:	
Change in aspartate transaminase (U/L)	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78 ^[40]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.58
upper limit	5.7
Variability estimate	Standard error of the mean

Notes:

[40] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES -Changes From Baseline to Visit 8 (Week 52) in Alanine aminotransferase (ALT)

End point title	EES -Changes From Baseline to Visit 8 (Week 52) in Alanine aminotransferase (ALT)
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in liver enzymes.	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: U/L				
arithmetic mean (standard deviation)	-3.26 (± 24.67)	-7.02 (± 36.21)	-12.54 (± 44.72)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Statistical analysis description: Change in alanine aminotransferase (U/L)	
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221 ^[41]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-6.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.97
upper limit	3.71
Variability estimate	Standard error of the mean

Notes:

[41] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description: Change in alanine aminotransferase (U/L)	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.062 ^[42]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-9.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.4
upper limit	0.49
Variability estimate	Standard error of the mean

Notes:

[42] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: CK 18-M65

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: CK 18-M65
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in CK 18-M65 (non-invasive markers of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: U/L				
arithmetic mean (standard deviation)	-45.53 (\pm 437.21)	104.04 (\pm 804.96)	-185.01 (\pm 658.14)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095 ^[43]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	141.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.99
upper limit	308.55
Variability estimate	Standard error of the mean

Notes:

[43] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.412 ^[44]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-70.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-239.85
upper limit	98.71
Variability estimate	Standard error of the mean

Notes:

[44] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: CK18 M30

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: CK18 M30
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in CK18 M30 (non-invasive markers of fibrosis and steatosis).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	78	
Units: pmol/L				
arithmetic mean (standard deviation)	-51.39 (± 349.64)	-28.08 (± 574.50)	-66.40 (± 432.02)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.592 ^[45]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	32.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-86.63
upper limit	151.42
Variability estimate	Standard error of the mean

Notes:

[45] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.61 ^[46]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	31.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-89.42
upper limit	152.12
Variability estimate	Standard error of the mean

Notes:

[46] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Adiponectin

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Adiponectin
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in adiponectin (non-invasive markers of fibrosis and steatosis).	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: µg/mL				
arithmetic mean (standard deviation)	2.54 (± 9.48)	4.98 (± 20.25)	1.90 (± 8.34)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459 ^[47]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.77
upper limit	6.11
Variability estimate	Standard error of the mean

Notes:

[47] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.764 ^[48]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	3.72
Variability estimate	Standard error of the mean

Notes:

[48] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Ferritin

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Ferritin
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in ferritin (non-invasive markers of fibrosis and steatosis).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	77	
Units: µg/L				
arithmetic mean (standard deviation)	-19.26 (± 122.57)	-23.52 (± 145.61)	-19.68 (± 81.91)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.466 ^[49]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-12.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.79
upper limit	21.95
Variability estimate	Standard error of the mean

Notes:

[49] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745 ^[50]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-5.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.07
upper limit	29.42
Variability estimate	Standard error of the mean

Notes:

[50] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: FG19

End point title	EES - Changes From Baseline to Week 52 in Non-invasive
------------------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in FG19 (non-invasive marker of fibrosis and steatosis).

End point type

Secondary

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: pg/mL				
arithmetic mean (standard deviation)	11.64 (\pm 87.10)	-27.25 (\pm 94.19)	-26.03 (\pm 91.59)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018 ^[51]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-26.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.59
upper limit	-4.54
Variability estimate	Standard error of the mean

Notes:

[51] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[52]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-40.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.61
upper limit	-18.17
Variability estimate	Standard error of the mean

Notes:

[52] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: FG21

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: FG21
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in FG21 (non-invasive marker of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: pg/mL				
arithmetic mean (standard deviation)	73.05 (± 360.41)	258.74 (± 1138.36)	319.68 (± 433.63)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101 ^[53]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	190.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.38
upper limit	417.52
Variability estimate	Standard error of the mean

Notes:

[53] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052 ^[54]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	228.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	458.82
Variability estimate	Standard error of the mean

Notes:

[54] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Alpha2 Macroglobulin

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Alpha2 Macroglobulin
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in alpha2 macroglobulin (a non-invasive marker of fibrosis and steatosis).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	76	
Units: g/L				
arithmetic mean (standard deviation)	0.01 (± 0.28)	-0.14 (± 0.29)	-0.26 (± 0.36)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[55]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.01
Variability estimate	Standard error of the mean

Notes:

[55] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.001 ^[56]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	-0.15
Variability estimate	Standard error of the mean

Notes:

[56] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Hyaluronic Acid

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Hyaluronic Acid
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in hyaluronic acid	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	78	
Units: ng/mL				
arithmetic mean (standard deviation)	12.49 (\pm 48.68)	26.12 (\pm 230.97)	12.14 (\pm 48.04)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.203 ^[57]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-16.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.07
upper limit	8.98
Variability estimate	Standard error of the mean

Notes:

[57] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.603 ^[58]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-6.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.49
upper limit	18.9
Variability estimate	Standard error of the mean

Notes:

[58] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: N-terminal Pro-peptide of Collagen Type III (PIIINP)

End point title	EES - Changes From Baseline to Week 52 in Non-invasive
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in N-terminal pro-peptide of collagen type III (PIIINP),

End point type Secondary

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	81	78	
Units: ng/mL				
arithmetic mean (standard deviation)	0.29 (± 4.87)	-0.50 (± 3.43)	-0.57 (± 3.75)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235 ^[59]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	0.48
Variability estimate	Standard error of the mean

Notes:

[59] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.193 ^[60]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	0.41
Variability estimate	Standard error of the mean

Notes:

[60] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Tissue Inhibitor of Matrix Metalloprotease-1 (TIMP-1)

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Tissue Inhibitor of Matrix Metalloprotease-1 (TIMP-1)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in tissue inhibitor of matrix metalloprotease-1 (TIMP-1)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	81	78	
Units: ng/mL				
arithmetic mean (standard deviation)	9.08 (± 49.54)	15.21 (± 35.38)	-6.32 (± 39.75)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.348 ^[61]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	6.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.81
upper limit	19.22
Variability estimate	Standard error of the mean

Notes:

[61] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029 ^[62]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-14.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.81
upper limit	1.51
Variability estimate	Standard error of the mean

Notes:

[62] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fibrotest

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fibrotest
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in fibrotest
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	77	
Units: score				
arithmetic mean (standard deviation)	-0.01 (± 0.1)	-0.06 (± 0.08)	-0.07 (± 0.09)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[63]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	-0.02
Variability estimate	Standard error of the mean

Notes:

[63] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[64]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	-0.02
Variability estimate	Standard error of the mean

Notes:

[64] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES- Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Steatotest

End point title	EES- Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Steatotest
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in Steatotest	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	81	77	
Units: Score				
arithmetic mean (standard deviation)	0.03 (\pm 0.11)	-0.09 (\pm 0.11)	-0.08 (\pm 0.15)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[65]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	-0.07
Variability estimate	Standard error of the mean

Notes:

[65] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[66]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	-0.07
Variability estimate	Standard error of the mean

Notes:

[66] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Angulo test

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Angulo test
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in angulo index

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	75	
Units: score				
arithmetic mean (standard deviation)	-0.01 (± 0.51)	0.06 (± 0.53)	-0.26 (± 0.57)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.471 ^[67]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.23
Variability estimate	Standard error of the mean

Notes:

[67] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 ^[68]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.08
Variability estimate	Standard error of the mean

Notes:

[68] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis:Enhanced Liver Fibrosis (ELF)

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis:Enhanced Liver Fibrosis (ELF)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in enhanced liver fibrosis (ELF)

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	78	
Units: score				
arithmetic mean (standard deviation)	0.08 (± 0.70)	-0.01 (± 0.54)	-0.01 (± 0.64)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
----------------------------	----------------------

Statistical analysis description:

Enhanced Liver Fibrosis

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.457 ^[69]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.07

Confidence interval

level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.12
Variability estimate	Standard error of the mean

Notes:

[69] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description: Enhanced Liver Fibrosis	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.428 ^[70]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.12
Variability estimate	Standard error of the mean

Notes:

[70] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fatty Liver Index (FLI)

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fatty Liver Index (FLI)
End point description: To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in fatty liver index (FLI)	
End point type	Secondary
End point timeframe: Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	77	
Units: score				
arithmetic mean (standard deviation)	1.34 (± 11.65)	-7.94 (± 11.74)	-7.81 (± 14.29)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
-----------------------------------	----------------------

Statistical analysis description:

Fatty Liver Index

Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[71]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-9.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.19
upper limit	-5.24
Variability estimate	Standard error of the mean

Notes:

[71] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Statistical analysis description:	
Fatty Liver Index	
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[72]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-9.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.12
upper limit	-5.04
Variability estimate	Standard error of the mean

Notes:

[72] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fibrometer

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Fibrometer
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in Fibrometer	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	71	81	74	
Units: score				
arithmetic mean (standard deviation)	0.02 (\pm 0.22)	0.04 (\pm 0.23)	0 (\pm 0.20)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.531 ^[73]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.09
Variability estimate	Standard error of the mean

Notes:

[73] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.638 ^[74]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.05
Variability estimate	Standard error of the mean

Notes:

[74] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Plasma Glucose

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Plasma Glucose
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in plasma glucose (to assess insulin resistance).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	75	82	78	
Units: mmol/L				
arithmetic mean (standard deviation)	0.67 (± 1.95)	0.17 (± 1.23)	0.22 (± 1.70)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077 ^[75]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.05
Variability estimate	Standard error of the mean

Notes:

[75] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.172 ^[76]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	0.16
Variability estimate	Standard error of the mean

Notes:

[76] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Glycosylated Haemoglobin A1c (HbA1c)

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Glycosylated Haemoglobin A1c (HbA1c)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in glycosylated haemoglobin A1c (HbA1c; to assess insulin resistance).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	81	77	
Units: percent				
arithmetic mean (standard deviation)	0.25 (± 0.69)	0.22 (± 0.56)	0.03 (± 0.70)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.732 ^[77]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.17
Variability estimate	Standard error of the mean

Notes:

[77] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.062 ^[78]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.01
Variability estimate	Standard error of the mean

Notes:

[78] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Fructosamine

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Fructosamine
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in fructosamine (to assess insulin resistance).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: µmol/L				
arithmetic mean (standard deviation)	11.29 (± 28.62)	16.27 (± 27.53)	-8.24 (± 28.21)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4 ^[79]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	3.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.89
upper limit	12.2
Variability estimate	Standard error of the mean

Notes:

[79] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[80]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-16.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.99
upper limit	-7.44
Variability estimate	Standard error of the mean

Notes:

[80] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Leptin

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Leptin
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in leptin (to assess insulin resistance).	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: ng/mL				
arithmetic mean (standard deviation)	3.01 (± 8.08)	-0.21 (± 9.55)	3.51 (± 10.67)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066 ^[81]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.79
upper limit	0.18
Variability estimate	Standard error of the mean

Notes:

[81] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.615 ^[82]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	3.77
Variability estimate	Standard error of the mean

Notes:

[82] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Insulin

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Insulin
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in insulin (to assess insulin resistance).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	78	
Units: pmol/L				
arithmetic mean (standard deviation)	8.92 (± 112.26)	-33.88 (± 189.64)	-26.12 (± 111.76)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.307 ^[83]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-17.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.88
upper limit	16.08
Variability estimate	Standard error of the mean

Notes:

[83] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213 ^[84]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-21.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.17
upper limit	12.34
Variability estimate	Standard error of the mean

Notes:

[84] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: C Peptide

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: C Peptide
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in C peptide (to assess insulin resistance).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	77	
Units: nmol/L				
arithmetic mean (standard deviation)	0.12 (± 0.58)	-0.17 (± 0.55)	-0.03 (± 0.48)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 ^[85]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	-0.08
Variability estimate	Standard error of the mean

Notes:

[85] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068 ^[86]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.01
Variability estimate	Standard error of the mean

Notes:

[86] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Homeostatic Model Assessment-insulin Resistance (HOMA-IR)

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Homeostatic Model Assessment-insulin Resistance (HOMA-IR)
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in homeostatic model assessment-insulin resistance (HOMA-IR; to assess insulin resistance).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	78	
Units: total HOMA IR				
arithmetic mean (standard deviation)	1.01 (± 4.96)	-1.10 (± 10.76)	-1 (± 6.86)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.448 ^[87]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.86
upper limit	1.27
Variability estimate	Standard error of the mean

Notes:

[87] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.267 ^[88]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.25
upper limit	0.9
Variability estimate	Standard error of the mean

Notes:

[88] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Insulin Resistance: Free Fatty Acids (FFA)

End point title	EES - Changes From Baseline to Week 52 in Insulin Resistance: Free Fatty Acids (FFA)
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in free fatty acids (FFA; to assess insulin resistance).	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	78	78	
Units: mmol/L				
arithmetic mean (standard deviation)	0.05 (± 0.26)	-0.04 (± 0.25)	-0.04 (± 0.24)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095 ^[89]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.01
Variability estimate	Standard error of the mean

Notes:

[89] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 ^[90]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	-0.01
Variability estimate	Standard error of the mean

Notes:

[90] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Inflammatory Markers: Fibrinogen

End point title	EES - Changes From Baseline to Week 52 in Inflammatory Markers: Fibrinogen
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in fibrinogen (inflammatory markers).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	75	82	76	
Units: g/L				
arithmetic mean (standard deviation)	-0.05 (± 0.66)	-0.37 (± 0.70)	-0.37 (± 0.79)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[91]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.17
Variability estimate	Standard error of the mean

Notes:

[91] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 ^[92]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.08
Variability estimate	Standard error of the mean

Notes:

[92] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES -Changes From Baseline to Week 52 in Inflammatory Markers: Haptoglobin

End point title	EES -Changes From Baseline to Week 52 in Inflammatory Markers: Haptoglobin
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in haptoglobin (inflammatory markers).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	81	77	
Units: g/L				
arithmetic mean (standard deviation)	0.09 (± 0.35)	-0.19 (± 0.32)	-0.20 (± 0.40)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[93]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	-0.15
Variability estimate	Standard error of the mean

Notes:

[93] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[94]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	-0.17
Variability estimate	Standard error of the mean

Notes:

[94] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Inflammatory Markers: Tumour Necrosis Factor Alpha

End point title	EES - Changes From Baseline to Week 52 in Inflammatory Markers: Tumour Necrosis Factor Alpha
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in tumour necrosis factor alpha (inflammatory markers).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	81	78	
Units: pg/mL				
arithmetic mean (standard deviation)	0.19 (± 10.46)	1.37 (± 6.14)	-2.45 (± 38.58)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.742 ^[95]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	4.06
Variability estimate	Standard error of the mean

Notes:

[95] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.107 ^[96]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	6.43
Variability estimate	Standard error of the mean

Notes:

[96] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Inflammatory Markers: interleukine 6

End point title	EES - Changes From Baseline to Week 52 in Inflammatory Markers: interleukine 6
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in interleukine 6 (inflammatory markers).	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	82	78	
Units: pg/mL				
arithmetic mean (standard deviation)	-0.06 (\pm 1.37)	0.37 (\pm 4.20)	-1.14 (\pm 10.33)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.362 ^[97]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	1.59
Variability estimate	Standard error of the mean

Notes:

[97] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.894 ^[98]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	1.18
Variability estimate	Standard error of the mean

Notes:

[98] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Inflammatory Markers: Plasminogen Activator Inhibitor 1 (PAI-1)

End point title	EES - Changes From Baseline to Week 52 in Inflammatory
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in plasminogen activator inhibitor 1 (PAI-1; inflammatory marker).

End point type

Secondary

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	66	68	77	
Units: ng/mL				
arithmetic mean (standard deviation)	-0.14 (± 4.74)	-0.51 (± 3.51)	0.21 (± 4.28)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.229 ^[99]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.48
Variability estimate	Standard error of the mean

Notes:

[99] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.463 ^[100]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	0.76
Variability estimate	Standard error of the mean

Notes:

[100] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Inflammatory Markers: C-Reactive Protein (CRP)

End point title	EES - Changes From Baseline to Week 52 in Inflammatory Markers: C-Reactive Protein (CRP)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to Week 52, in C-Reactive Protein (CRP; inflammatory marker).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: log (mg/L)				
arithmetic mean (standard deviation)	0.20 (± 0.74)	-0.04 (± 0.72)	-0.05 (± 0.81)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065 ^[101]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.01
Variability estimate	Standard error of the mean

Notes:

[101] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.098 ^[102]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.03
Variability estimate	Standard error of the mean

Notes:

[102] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population - Changes From Baseline to Week 52 in Safety Markers: N-terminal Prohormone of Brain Natriuretic Peptide (NTproBNP; Cardiac Function Parameter)

End point title	Safety population - Changes From Baseline to Week 52 in Safety Markers: N-terminal Prohormone of Brain Natriuretic Peptide (NTproBNP; Cardiac Function Parameter)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in N-terminal prohormone of brain natriuretic peptide (NT-proBNP; safety marker; cardiac function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	93	
Units: pmol/L				
arithmetic mean (standard deviation)	-1.24 (± 5.35)	0.38 (± 4.81)	1.54 (± 4.16)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg

Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[103]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	3.72
Variability estimate	Standard error of the mean

Notes:

[103] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019 ^[104]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	2.91
Variability estimate	Standard error of the mean

Notes:

[104] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population - Changes From Baseline to Week 52 in Safety Markers: Troponin T (Cardiac Function Parameter)

End point title	Safety population - Changes From Baseline to Week 52 in Safety Markers: Troponin T (Cardiac Function Parameter)
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in troponin T (safety marker; cardiac function parameter).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	92	
Units: µg/L				
arithmetic mean (standard deviation)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.447 ^[105]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0
Variability estimate	Standard error of the mean

Notes:

[105] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.758 ^[106]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0
Variability estimate	Standard error of the mean

Notes:

[106] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population -Changes From Baseline to Week 52 in Safety Markers: Creatinine (Renal Function Parameter)

End point title	Safety population -Changes From Baseline to Week 52 in Safety Markers: Creatinine (Renal Function Parameter)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in creatinine (safety markers; renal function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	89	93	
Units: µmol/L				
arithmetic mean (standard deviation)	1.27 (± 7.85)	5.61 (± 8.18)	2.03 (± 7.89)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.553 ^[107]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	3.01
Variability estimate	Standard error of the mean

Notes:

[107] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[108]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	4.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.97
upper limit	6.64
Variability estimate	Standard error of the mean

Notes:

[108] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population - Changes From Baseline to Week 52 in Safety Markers: Creatinine Clearance (Renal Function Parameter)

End point title	Safety population - Changes From Baseline to Week 52 in Safety Markers: Creatinine Clearance (Renal Function Parameter)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in creatinine clearance (safety marker; renal function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	89	93	
Units: mL/min				
arithmetic mean (standard deviation)	-0.09 (± 0.62)	-0.56 (± 2.22)	-0.06 (± 0.94)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.861 ^[109]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.44
Variability estimate	Standard error of the mean

Notes:

[109] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052 ^[110]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	0
Variability estimate	Standard error of the mean

Notes:

[110] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population - Changes From Baseline to Week 52 in Safety Markers: Uric Acid (Renal Function Parameter)

End point title	Safety population - Changes From Baseline to Week 52 in Safety Markers: Uric Acid (Renal Function Parameter)
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in uric acid (safety marker; renal function parameter).
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	89	93	
Units: mmol/L				
arithmetic mean (standard deviation)	-0.01 (± 0.06)	0.01 (± 0.05)	0 (± 0.06)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473 ^[111]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.02
Variability estimate	Standard error of the mean

Notes:

[111] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.124 ^[112]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.03
Variability estimate	Standard error of the mean

Notes:

[112] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population - Changes From Baseline to Week 52 in Safety Markers: Blood Urea Nitrogen (BUN; Renal Function Parameter)

End point title	Safety population - Changes From Baseline to Week 52 in Safety Markers: Blood Urea Nitrogen (BUN; Renal Function Parameter)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in blood urea nitrogen (BUN; safety marker; renal function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	89	93	
Units: mmol urea/L				
arithmetic mean (standard deviation)	-0.17 (± 1.14)	0.67 (± 1.22)	0.61 (± 1.28)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[113]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.15
Variability estimate	Standard error of the mean

Notes:

[113] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[114]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.19
Variability estimate	Standard error of the mean

Notes:

[114] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population -Changes From Baseline to Week 52 in Safety Markers: Cystatin C (Renal Function Parameter)

End point title	Safety population -Changes From Baseline to Week 52 in Safety Markers: Cystatin C (Renal Function Parameter)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in cystatin C (safety marker; renal function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	93	
Units: mg/L				
arithmetic mean (standard deviation)	0.04 (± 0.13)	0.04 (± 0.22)	0.05 (± 0.10)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	GFT505 80mg v Placebo
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.842 ^[115]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.04
Variability estimate	Standard error of the mean

Notes:

[115] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.589 ^[116]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.05
Variability estimate	Standard error of the mean

Notes:

[116] - Baseline parameter value and presence of diabetes as random factors

Secondary: Safety population -Changes From Baseline to Week 52 in Safety Markers: Beta2-microglobulin (Renal Function Parameter)

End point title	Safety population -Changes From Baseline to Week 52 in Safety Markers: Beta2-microglobulin (Renal Function Parameter)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to week 52, in beta2-microglobulin (safety marker; renal function parameter).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	Placebo	GFT505 120mg	GFT505 80mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	93	
Units: µg/L				
arithmetic mean (standard deviation)	-83.48 (± 279.31)	0.11 (± 466.43)	-22.26 (± 326.42)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	Placebo v GFT505 80mg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.325 ^[117]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	48.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.73
upper limit	146.6
Variability estimate	Standard error of the mean

Notes:

[117] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	Placebo v GFT505 120mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066 ^[118]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	93.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.06
upper limit	192.49
Variability estimate	Standard error of the mean

Notes:

[118] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES -Changes From Baseline to Week 52 in Body Weight

End point title	EES -Changes From Baseline to Week 52 in Body Weight
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg, or GFT505 120mg, the changes from baseline to Week 52, in body weight.
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: kilogram(s)				
arithmetic mean (standard deviation)	-0.04 (± 3.4)	0.11 (± 3.61)	-0.69 (± 4.09)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.942 ^[119]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	1.04
Variability estimate	Standard error of the mean

Notes:

[119] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.304 ^[120]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	1.66
Variability estimate	Standard error of the mean

Notes:

[120] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo A1

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo A1
End point description:	
To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry	
End point type	Secondary
End point timeframe:	
Baseline (Visit 2; Week 0) to Visit 8 (Week 52)	

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: mg/dL				
arithmetic mean (standard deviation)	-3.90 (\pm 16.53)	1.63 (\pm 15.59)	2.85 (\pm 20.42)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038 ^[121]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	11.14
Variability estimate	Standard error of the mean

Notes:

[121] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 ^[122]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	7.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.59
upper limit	12.55
Variability estimate	Standard error of the mean

Notes:

[122] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo B

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

End point type Secondary

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: mg/dL				
arithmetic mean (standard deviation)	0.94 (\pm 14.29)	-12.80 (\pm 20.87)	-8.42 (\pm 16.03)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[123]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-12.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.56
upper limit	-7.25
Variability estimate	Standard error of the mean

Notes:

[123] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[124]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-9.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.81
upper limit	-4.41
Variability estimate	Standard error of the mean

Notes:

[124] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo AII

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo AII
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	-3.36 (± 4.82)	-0.15 (± 6.63)	4.25 (± 4.36)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[125]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	3.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.14
upper limit	4.96
Variability estimate	Standard error of the mean

Notes:

[125] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[126]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.67
upper limit	7.53
Variability estimate	Standard error of the mean

Notes:

[126] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	0.77 (± 4.30)	-1.79 (± 3.91)	-0.69 (± 3.42)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[127]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-2.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.29
upper limit	-1.25
Variability estimate	Standard error of the mean

Notes:

[127] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[128]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.5

Confidence interval

level	95 %
sides	2-sided
lower limit	-2.52
upper limit	-0.49
Variability estimate	Standard error of the mean

Notes:

[128] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES -Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII/B

End point title	EES -Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII/B
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	0.53 (± 3.05)	-1.44 (± 2.98)	-0.65 (± 2.98)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[129]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	-0.92
Variability estimate	Standard error of the mean

Notes:

[129] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 ^[130]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.29
Variability estimate	Standard error of the mean

Notes:

[130] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII/nonB

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo CIII/nonB
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	0.24 (\pm 2.53)	-0.35 (\pm 1.79)	-0.04 (\pm 0.76)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[131]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.17
Variability estimate	Standard error of the mean

Notes:

[131] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 ^[132]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.1
Variability estimate	Standard error of the mean

Notes:

[132] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry Small dense Low Density Lipoproteins

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry Small dense Low Density Lipoproteins
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	69	71	69	
Units: mg/dL				
arithmetic mean (standard deviation)	0.60 (± 7.52)	-2.09 (± 11.02)	-2.62 (± 6.08)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069 ^[133]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.89
upper limit	0.19
Variability estimate	Standard error of the mean

Notes:

[133] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 ^[134]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-3.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.95
upper limit	-0.84
Variability estimate	Standard error of the mean

Notes:

[134] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Lp(a)

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Lp(a)
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	0.80 (± 4.46)	-0.57 (± 12.24)	-0.91 (± 13.75)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.549 ^[135]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	3.61
Variability estimate	Standard error of the mean

Notes:

[135] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.728 ^[136]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.28
upper limit	3.26
Variability estimate	Standard error of the mean

Notes:

[136] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry Apo E

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry Apo E
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	-0.29 (± 3.67)	-1.72 (± 2.75)	-1.38 (± 2.99)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- GFT505 80mg v EES (ITT)- Placebo

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[137]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	-0.61
Variability estimate	Standard error of the mean

Notes:

[137] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[138]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	-0.36
Variability estimate	Standard error of the mean

Notes:

[138] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo E/B

End point title	EES - Changes From Baseline to Week 52 in Outcomes Related to Biochemistry: Apo E/B
End point description:	To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg the changes from baseline to week 52, in secondary outcomes related to biochemistry
End point type	Secondary
End point timeframe:	Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	66	65	
Units: mg/dL				
arithmetic mean (standard deviation)	-0.21 (± 2.59)	-1.43 (± 2.43)	-1.48 (± 2.64)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[139]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	-0.53
Variability estimate	Standard error of the mean

Notes:

[139] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 ^[140]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.72
upper limit	-0.43
Variability estimate	Standard error of the mean

Notes:

[140] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Prothrombin Ratio

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: Prothrombin Ratio
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in prothrombin ratio (non-invasive marker of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	75	82	76	
Units: Ratio				
arithmetic mean (standard deviation)	0.51 (\pm 14.28)	-3.85 (\pm 11.57)	1.29 (\pm 10.03)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075 ^[141]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-2.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.95
upper limit	0.29
Variability estimate	Standard error of the mean

Notes:

[141] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.491 ^[142]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-1.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.29
upper limit	2.07
Variability estimate	Standard error of the mean

Notes:

[142] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: total bilirubin

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: total bilirubin
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in total bilirubin (non-invasive markers of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: µmol/L				
arithmetic mean (standard deviation)	-1.46 (± 3.77)	-1.53 (± 3.66)	-1.38 (± 4.85)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.831 ^[143]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	1.12
Variability estimate	Standard error of the mean

Notes:

[143] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.754 ^[144]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	1.47
Variability estimate	Standard error of the mean

Notes:

[144] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES -Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: conjugated bilirubin

End point title	EES -Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: conjugated bilirubin
-----------------	---

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in conjugated bilirubin (non-invasive markers of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	77	82	78	
Units: µmol/L				
arithmetic mean (standard deviation)	-0.26 (± 1.05)	-0.35 (± 1.26)	-0.15 (± 1.24)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.848 ^[145]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.3
Variability estimate	Standard error of the mean

Notes:

[145] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.511 ^[146]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	0.11

Confidence interval

level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.45
Variability estimate	Standard error of the mean

Notes:

[146] - Baseline parameter value and presence of diabetes as random factors

Secondary: EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: International Normalized Ratio (INR)

End point title	EES - Changes From Baseline to Week 52 in Non-invasive Markers of Fibrosis and Steatosis: International Normalized Ratio (INR)
-----------------	--

End point description:

To evaluate after 52 weeks of daily administration of GFT505 80mg or GFT505 120mg, the changes from baseline to week 52, in international normalized ratio (INR; non-invasive marker of fibrosis and steatosis).

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

End point timeframe:

Baseline (Visit 2; Week 0) to Visit 8 (Week 52)

End point values	EES (ITT)- Placebo	EES (ITT)- GFT505 80mg	EES (ITT)- GFT505 120mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	75	82	76	
Units: INR				
arithmetic mean (standard deviation)	0.03 (± 0.39)	0.03 (± 0.09)	-0.01 (± 0.08)	

Statistical analyses

Statistical analysis title	GFT505 80mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 80mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.393 ^[147]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.04
Variability estimate	Standard error of the mean

Notes:

[147] - Baseline parameter value and presence of diabetes as random factors

Statistical analysis title	GFT505 120mg, Placebo
Comparison groups	EES (ITT)- Placebo v EES (ITT)- GFT505 120mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.289 ^[148]
Method	Mixed models analysis
Parameter estimate	difference in least square mean change
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.03
Variability estimate	Standard error of the mean

Notes:

[148] - Baseline parameter value and presence of diabetes as random factors

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event information was collected at every study visit from screening up to the termination of the study corresponding to 64 weeks.

Adverse event reporting additional description:

The investigator established whether or not any AE had occurred at each visit (from the date of consent to the last visit). The participant was questioned in a general manner to determine specific symptoms without offering the patient any suggestion. Serious AE reporting began from signature of the participant ICF and ended at the last study visit.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	GFT505 80mg Safety Population
-----------------------	-------------------------------

Reporting group description: -

Reporting group title	GFT505 120mg Safety Population
-----------------------	--------------------------------

Reporting group description: -

Reporting group title	Placebo Safety Population
-----------------------	---------------------------

Reporting group description: -

Serious adverse events	GFT505 80mg Safety Population	GFT505 120mg Safety Population	Placebo Safety Population
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 93 (12.90%)	14 / 89 (15.73%)	9 / 92 (9.78%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			

subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Renal cancer			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroidectomy			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device breakage			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Psychotic disorder			

subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Overdose			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Radius fracture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			

subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle contractions involuntary			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 93 (0.00%)	2 / 89 (2.25%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder diverticulum			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nephrolithiasis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Osteoarthritis			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 93 (1.08%)	0 / 89 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Gastroenteritis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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

Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 89 (1.12%)	0 / 92 (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

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	GFT505 80mg Safety Population	GFT505 120mg Safety Population	Placebo Safety Population
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 93 (91.40%)	86 / 89 (96.63%)	85 / 92 (92.39%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 93 (5.38%)	7 / 89 (7.87%)	4 / 92 (4.35%)
occurrences (all)	5	7	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 93 (7.53%)	0 / 89 (0.00%)	5 / 92 (5.43%)
occurrences (all)	10	0	6
Chest pain			
subjects affected / exposed	4 / 93 (4.30%)	7 / 89 (7.87%)	3 / 92 (3.26%)
occurrences (all)	5	7	3
Fatigue			
subjects affected / exposed	13 / 93 (13.98%)	12 / 89 (13.48%)	14 / 92 (15.22%)
occurrences (all)	15	14	16
Influenza like illness			
subjects affected / exposed	1 / 93 (1.08%)	4 / 89 (4.49%)	1 / 92 (1.09%)
occurrences (all)	1	4	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed occurrences (all)	4 / 93 (4.30%) 4	0 / 89 (0.00%) 0	1 / 92 (1.09%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 93 (2.15%) 2	6 / 89 (6.74%) 6	5 / 92 (5.43%) 5
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	6 / 93 (6.45%) 7 5 / 93 (5.38%) 5 5 / 93 (5.38%) 5	4 / 89 (4.49%) 4 5 / 89 (5.62%) 5 2 / 89 (2.25%) 2	1 / 92 (1.09%) 1 1 / 92 (1.09%) 1 4 / 92 (4.35%) 4
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Glycosylated haemoglobin increased subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all)	4 / 93 (4.30%) 6 1 / 93 (1.08%) 1 1 / 93 (1.08%) 1 4 / 93 (4.30%) 4	7 / 89 (7.87%) 7 4 / 89 (4.49%) 4 4 / 89 (4.49%) 4 3 / 89 (3.37%) 3	2 / 92 (2.17%) 2 0 / 92 (0.00%) 0 2 / 92 (2.17%) 2 3 / 92 (3.26%) 3
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	6 / 93 (6.45%) 6	11 / 89 (12.36%) 11	10 / 92 (10.87%) 11
Nervous system disorders			

Dizziness			
subjects affected / exposed	10 / 93 (10.75%)	6 / 89 (6.74%)	9 / 92 (9.78%)
occurrences (all)	12	6	9
Headache			
subjects affected / exposed	16 / 93 (17.20%)	12 / 89 (13.48%)	15 / 92 (16.30%)
occurrences (all)	23	14	17
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	9 / 93 (9.68%)	11 / 89 (12.36%)	11 / 92 (11.96%)
occurrences (all)	11	12	12
Abdominal pain upper			
subjects affected / exposed	12 / 93 (12.90%)	9 / 89 (10.11%)	13 / 92 (14.13%)
occurrences (all)	14	11	15
Constipation			
subjects affected / exposed	7 / 93 (7.53%)	5 / 89 (5.62%)	5 / 92 (5.43%)
occurrences (all)	8	5	5
Diarrhoea			
subjects affected / exposed	14 / 93 (15.05%)	9 / 89 (10.11%)	6 / 92 (6.52%)
occurrences (all)	17	9	6
Dyspepsia			
subjects affected / exposed	0 / 93 (0.00%)	4 / 89 (4.49%)	4 / 92 (4.35%)
occurrences (all)	0	4	4
Flatulence			
subjects affected / exposed	2 / 93 (2.15%)	1 / 89 (1.12%)	4 / 92 (4.35%)
occurrences (all)	2	1	4
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 93 (2.15%)	2 / 89 (2.25%)	7 / 92 (7.61%)
occurrences (all)	3	2	7
Nausea			
subjects affected / exposed	18 / 93 (19.35%)	17 / 89 (19.10%)	14 / 92 (15.22%)
occurrences (all)	23	20	16
Vomiting			
subjects affected / exposed	7 / 93 (7.53%)	8 / 89 (8.99%)	9 / 92 (9.78%)
occurrences (all)	8	9	12
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	1 / 93 (1.08%) 1	2 / 89 (2.25%) 2	4 / 92 (4.35%) 4
Hyperhidrosis subjects affected / exposed occurrences (all)	3 / 93 (3.23%) 3	4 / 89 (4.49%) 4	2 / 92 (2.17%) 2
Pruritus subjects affected / exposed occurrences (all)	3 / 93 (3.23%) 4	2 / 89 (2.25%) 2	4 / 92 (4.35%) 4
Rash subjects affected / exposed occurrences (all)	6 / 93 (6.45%) 8	6 / 89 (6.74%) 6	4 / 92 (4.35%) 4
Renal and urinary disorders Glycosuria subjects affected / exposed occurrences (all)	1 / 93 (1.08%) 1	6 / 89 (6.74%) 6	3 / 92 (3.26%) 3
Leukocyturia subjects affected / exposed occurrences (all)	10 / 93 (10.75%) 12	8 / 89 (8.99%) 9	12 / 92 (13.04%) 17
Proteinuria subjects affected / exposed occurrences (all)	1 / 93 (1.08%) 1	2 / 89 (2.25%) 2	6 / 92 (6.52%) 6
Renal failure subjects affected / exposed occurrences (all)	1 / 93 (1.08%) 1	4 / 89 (4.49%) 5	0 / 92 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	7 / 93 (7.53%) 7	9 / 89 (10.11%) 10	6 / 92 (6.52%) 9
Back pain subjects affected / exposed occurrences (all)	7 / 93 (7.53%) 9	9 / 89 (10.11%) 9	8 / 92 (8.70%) 9
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	4 / 93 (4.30%) 4	0 / 89 (0.00%) 0	0 / 92 (0.00%) 0
Muscle spasms			

subjects affected / exposed	2 / 93 (2.15%)	3 / 89 (3.37%)	6 / 92 (6.52%)
occurrences (all)	2	3	7
Myalgia			
subjects affected / exposed	9 / 93 (9.68%)	3 / 89 (3.37%)	3 / 92 (3.26%)
occurrences (all)	9	5	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 93 (10.75%)	6 / 89 (6.74%)	8 / 92 (8.70%)
occurrences (all)	11	6	8
Influenza			
subjects affected / exposed	10 / 93 (10.75%)	3 / 89 (3.37%)	5 / 92 (5.43%)
occurrences (all)	12	3	6
Gastroenteritis			
subjects affected / exposed	4 / 93 (4.30%)	2 / 89 (2.25%)	0 / 92 (0.00%)
occurrences (all)	4	3	0
Nasopharyngitis			
subjects affected / exposed	9 / 93 (9.68%)	5 / 89 (5.62%)	5 / 92 (5.43%)
occurrences (all)	13	6	5
Sinusitis			
subjects affected / exposed	5 / 93 (5.38%)	9 / 89 (10.11%)	2 / 92 (2.17%)
occurrences (all)	5	11	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 93 (1.08%)	4 / 89 (4.49%)	5 / 92 (5.43%)
occurrences (all)	1	5	5
Urinary tract infection			
subjects affected / exposed	6 / 93 (6.45%)	6 / 89 (6.74%)	3 / 92 (3.26%)
occurrences (all)	10	6	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 93 (4.30%)	5 / 89 (5.62%)	1 / 92 (1.09%)
occurrences (all)	4	5	1
Diabetes mellitus inadequate control			
subjects affected / exposed	5 / 93 (5.38%)	4 / 89 (4.49%)	5 / 92 (5.43%)
occurrences (all)	7	5	5
Hyperglycaemia			

subjects affected / exposed	1 / 93 (1.08%)	2 / 89 (2.25%)	4 / 92 (4.35%)
occurrences (all)	1	2	4
Hyperlipidaemia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 89 (0.00%)	7 / 92 (7.61%)
occurrences (all)	0	0	7
Hypertriglyceridaemia			
subjects affected / exposed	5 / 93 (5.38%)	3 / 89 (3.37%)	3 / 92 (3.26%)
occurrences (all)	5	3	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2012	In amendment n°1, main substantial modifications concerned the protocol title, possibility of realization of biology B1 30 days before the liver biopsy, the inclusion criterion n°3 (addition of specific contraceptive measures for male participants and female partner), the list of non-permitted medications (removal of CYP2C9), and modification of discontinuation criteria (stopping rules are no more applicable).
28 June 2013	In amendment n°2, main substantial modifications concerned extension of the delay for historical liver biopsies to 9 months, change related to B1 scheduling for patients having a historical liver biopsy and modification of the list of non-permitted medications (removal of CYP2C19).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported