



Clinical trial results:

Single (open-label) and repeat dose (randomized, placebo-controlled) trial to assess the safety, tolerability and pharmacokinetics of GB1211 (Gal-3 inhibitor) in participants with hepatic impairment (Child-Pugh B and Child-Pugh C).

Summary

EudraCT number	2021-001235-12
Trial protocol	BG
Global end of trial date	04 July 2022

Results information

Result version number	v1 (current)
This version publication date	21 September 2023
First version publication date	21 September 2023

Trial information

Trial identification

Sponsor protocol code	GULLIVER-2
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05009680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galecto Biotech AB
Sponsor organisation address	Cobis Science Park Ole Maaloes Vej 3, Copenhagen, Denmark, DK-2200
Public contact	Chief Medical Officer , Galecto Biotech AB, Clinicaltrials@galecto.com
Scientific contact	Chief Medical Officer , Galecto Biotech AB, Clinicaltrials@galecto.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2022
Global end of trial reached?	Yes
Global end of trial date	04 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective (Part 1, 2 and 3):

To assess the effect of hepatic impairment on the safety, tolerability and pharmacokinetics of GB1211 in participants with moderate or severe hepatic impairment.

Secondary objectives (Part 2):

To assess the effect of GB1211 on hepatic function in participants with moderate hepatic impairment.

Protection of trial subjects:

This study was conducted in accordance with the International Council on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	46

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Male or female subjects between 18 and 75 years with moderate hepatic impairment as defined by Child-Pugh B score, with severe hepatic impairment as defined by the Child-Pugh C score and healthy participants (controls).

Pre-assignment

Screening details:

Demographics; Medical and surgical history; Inclusion and exclusion criteria; Physical examination; Recording body weight and height; Vital signs; 12-lead ECG; Safety laboratory; Serum pregnancy test; Alcohol breath test; Urine drug screen; Prior and Concomitant medication; AEs; SARS-CoV-2 antigen; Serology; (LiMAX test and FibroScan in Part 2).

Period 1

Period 1 title	Baseline Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)

Arm description:

Subjects with moderate hepatic impairment (Child-Pugh B) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Arm title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
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Arm description:

Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.

Arm type	Matching control
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Arm title	Part 2 GB1211 100 mg (2 x 50 mg)
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Arm description:

Subjects with moderate hepatic impairment (Child-Pugh B) received GB1211, 100 mg (2 x 50 mg capsules of GB1211), twice daily for 12 weeks.

Arm type	Experimental
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Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Orally administered 100 mg GB1211 (2 x 50 mg, capsule), twice daily.	
Arm title	Part 2 Placebo (2 x 0 mg)
Arm description:	
Subjects with moderate hepatic impairment (Child-Pugh B) received Placebo (2 x 0 mg, capsule), twice daily for 12 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	P
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Orally administered Placebo (2 x 0 mg, capsule), twice daily.	
Arm title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Arm description:	
Subjects with severe hepatic impairment (Child-Pugh C) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.	
Arm title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Arm description:	
Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Arm type	Matching control
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.	

Number of subjects in period 1	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)	Part 2 GB1211 100 mg (2 x 50 mg)
Started	6	6	15
Completed	6	6	13
Not completed	0	0	2
Adverse event, serious fatal	-	-	1
Withdrawal of informed consent	-	-	1

Number of subjects in period 1	Part 2 Placebo (2 x 0 mg)	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Started	15	6	6
Completed	15	6	6
Not completed	0	0	0
Adverse event, serious fatal	-	-	-
Withdrawal of informed consent	-	-	-

Period 2

Period 2 title	PART 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Part 2 of this study was a double-blinded trial. During the clinical phase of the trial, neither the subjects nor the site personnel involved in the study assessments were aware of the identity of the treatments administered (GB1211 or Placebo). Blinding was ensured by the Interactive Web-based Response System (IWRS) and was to be broken by a PI only for specific subjects where there was a reason to do.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 2 GB1211 100 mg (2 x 50 mg)

Arm description:

Subjects with moderate hepatic impairment (Child-Pugh B) received GB1211, 100 mg (2 x 50 mg capsules of GB1211), twice daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), twice daily.

Arm title	Part 2 Placebo (2 x 0 mg)
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Arm description:

Subjects with moderate hepatic impairment (Child-Pugh B) received Placebo (2 x 0 mg, capsule), twice daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	P
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered Placebo (2 x 0 mg, capsule), twice daily.

Number of subjects in period 2^[1]	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)
Started	15	15
Completed	13	15
Not completed	2	0
Adverse event, serious fatal	1	-
Withdrawal of informed consent	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Period 1 and period 2 had different enrolled population.

Period 3

Period 3 title	PART 1
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)

Arm description:

Subjects with moderate hepatic impairment (Child-Pugh B) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Arm title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
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Arm description:

Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.

Arm type	Matching control
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Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Number of subjects in period 3^[2]	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Started	6	6
Completed	6	6

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Period 2 and period 3 had different enrolled population.

Period 4

Period 4 title	PART 3
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)

Arm description:

Subjects with severe hepatic impairment (Child-Pugh C) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Arm title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
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Arm description:

Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.

Arm type	Matching control
Investigational medicinal product name	Test product
Investigational medicinal product code	T
Other name	GB1211
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Orally administered 100 mg GB1211 (2 x 50 mg, capsule), single dose.

Number of subjects in period 4	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Started	6	6
Completed	6	6

Baseline characteristics

Reporting groups

Reporting group title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Reporting group title	Part 2 GB1211 100 mg (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received GB1211, 100 mg (2 x 50 mg capsules of GB1211), twice daily for 12 weeks.	
Reporting group title	Part 2 Placebo (2 x 0 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received Placebo (2 x 0 mg, capsule), twice daily for 12 weeks.	
Reporting group title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with severe hepatic impairment (Child-Pugh C) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	

Reporting group values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)	Part 2 GB1211 100 mg (2 x 50 mg)
Number of subjects	6	6	15
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	6	11
From 65-84 years	1	0	4
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.67	51.50	58.07
standard deviation	± 8.04	± 7.42	± 6.33
Gender categorical Units: Subjects			
Female	2	2	5
Male	4	4	10

Race			
Units: Subjects			
White	6	6	15
Height			
Units: cm			
arithmetic mean	170.17	167.67	168.80
standard deviation	± 7.81	± 5.57	± 9.32
Weight			
Units: kg			
arithmetic mean	64.12	65.23	87.12
standard deviation	± 11.62	± 12.74	± 20.92
BMI			
Units: (kg/m2)			
arithmetic mean	22.22	23.37	30.51
standard deviation	± 4.69	± 5.45	± 6.68

Reporting group values	Part 2 Placebo (2 x 0 mg)	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects	15	6	6
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	6	5
From 65-84 years	2	0	1
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	52.53	58.33	57.00
standard deviation	± 6.81	± 4.63	± 7.64
Gender categorical			
Units: Subjects			
Female	5	2	2
Male	10	4	4
Race			
Units: Subjects			
White	15	6	6
Height			
Units: cm			
arithmetic mean	174.13	168.17	174.83
standard deviation	± 7.61	± 7.14	± 10.09
Weight			
Units: kg			
arithmetic mean	76.33	79.00	86.90
standard deviation	± 18.76	± 17.15	± 21.66
BMI			

Units: (kg/m2)			
arithmetic mean	25.06	27.93	28.13
standard deviation	± 5.60	± 6.05	± 5.00
Reporting group values	Total		
Number of subjects	54		
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)	46		
From 65-84 years	8		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	18		
Male	36		
Race			
Units: Subjects			
White	54		
Height			
Units: cm			
arithmetic mean			
standard deviation	-		
Weight			
Units: kg			
arithmetic mean			
standard deviation	-		
BMI			
Units: (kg/m2)			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Reporting group title	Part 2 GB1211 100 mg (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received GB1211, 100 mg (2 x 50 mg capsules of GB1211), twice daily for 12 weeks.	
Reporting group title	Part 2 Placebo (2 x 0 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received Placebo (2 x 0 mg, capsule), twice daily for 12 weeks.	
Reporting group title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with severe hepatic impairment (Child-Pugh C) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Reporting group title	Part 2 GB1211 100 mg (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received GB1211, 100 mg (2 x 50 mg capsules of GB1211), twice daily for 12 weeks.	
Reporting group title	Part 2 Placebo (2 x 0 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received Placebo (2 x 0 mg, capsule), twice daily for 12 weeks.	
Reporting group title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with moderate hepatic impairment (Child-Pugh B) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Reporting group title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Reporting group description: Subjects with severe hepatic impairment (Child-Pugh C) received single oral dose of 100 mg GB1211 (2 x 50 mg capsule) on Day 1.	
Reporting group title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Reporting group description: Healthy Subjects received single oral dose of 100 mg GB1211 (2 x 50 mg) on Day 1.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: The safety population included all participants who received at least 1 dose of study treatment (GB1211 or placebo). The safety population was used for summaries of safety and other (such as disposition, concomitant medications, etc.) variables and for all safety analyses. The participants in the safety	

population were analyzed according to the treatment they have received.

Subject analysis set title	PK Population
Subject analysis set type	Per protocol

Subject analysis set description:

The PK population in Part 2 included all participants who received GB1211 and had enough quantifiable PK samples to estimate the PK profiles on at least one out of Days 1 and 21 and who had no important protocol deviations affecting the PK parameters. The PK population was used for the descriptive summaries and statistical analyses of the PK concentrations and parameters.

Subject analysis set title	mITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population included all participants who were randomized and received study treatment (GB1211 or placebo) for the 12-week planned dosing period. The participants in the mITT population were analyzed according to the treatment to which they were randomized. Note: this population was defined post hoc.

Subject analysis set title	Per Protocol (PP) Population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population included all participants who were randomized, received at least 1 dose of study treatment (GB1211 or placebo) and who had no important protocol deviations. Each participant in the PP population was analyzed according to the treatment they had received.

Primary: Part 2 AUC(0- τ),ss (total GB1211)

End point title	Part 2 AUC(0- τ),ss (total GB1211) ^[1]
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End point description:

Area under the total plasma concentration versus time curve during a dosage interval τ at steady state.

End point type	Primary
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End point timeframe:

From time 0 to dosage interval τ at steady state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: (h.ng/mL)				
arithmetic mean (standard deviation)	15494.72 (\pm 10708.99)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 AUC(0- τ) (total GB1211)

End point title	Part 2 AUC(0- τ) (total GB1211) ^[2]
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End point description:

Area under the total plasma concentration versus time curve during a dosage interval τ .

End point type	Primary
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End point timeframe:

From time 0 to dosage interval tau.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: h.ng/mL				
arithmetic mean (standard deviation)	4259.38 (± 2211.40)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cmax,ss (total GB1211)

End point title | Part 2 Cmax,ss (total GB1211)^[3]

End point description:

Maximum measured total plasma drug concentration at steady-state (on Day 21).

End point type | Primary

End point timeframe:

From time zero to t at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	1910.91 (± 1078.13)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cmax (total GB1211)

End point title | Part 2 Cmax (total GB1211)^[4]

End point description:

Maximum measured total plasma drug concentration.

End point type | Primary

End point timeframe:

From time zero to t.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: ng/mL				
arithmetic mean (standard deviation)	636.86 (\pm 334.89)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cmin,ss (total GB1211)

End point title Part 2 Cmin,ss (total GB1211)^[5]

End point description:

Minimum measured total plasma drug concentration at steady-state (on Day 21).

End point type Primary

End point timeframe:

From time zero to t at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	813.30 (\pm 586.74)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cav,ss (total GB1211)

End point title Part 2 Cav,ss (total GB1211)^[6]

End point description:

Average total plasma concentration at steady-state (on Day 21).

End point type Primary

End point timeframe:

At steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	1291.23 (\pm 892.42)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 CLss/F (total GB1211)

End point title Part 2 CLss/F (total GB1211)^[7]

End point description:

Apparent oral clearance at steady-state.

End point type Primary

End point timeframe:

From time 0 to dosage interval tau at steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: L/h				
arithmetic mean (standard deviation)	9.11 (\pm 5.30)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 CL/F (total GB1211)

End point title Part 2 CL/F (total GB1211)^[8]

End point description:

Apparent oral clearance.

End point type Primary

End point timeframe:

From time 0 to dosage interval tau.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: L/h				
median (full range (min-max))	12.80 (12.80 to 12.80)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Vzss/F (total GB1211)

End point title	Part 2 Vzss/F (total GB1211) ^[9]
End point description:	
Apparent volume of distribution at steady-state.	
End point type	Primary
End point timeframe:	
From time 0 to dosage interval τ at steady state.	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: litre(s)				
arithmetic mean (standard deviation)	108.38 (\pm 52.26)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Vz/F (total GB1211)

End point title	Part 2 Vz/F (total GB1211) ^[10]
End point description:	
Apparent volume of distribution.	
End point type	Primary
End point timeframe:	
From time 0 to dosage interval τ .	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: litre(s)				
median (full range (min-max))	382.75 (382.75 to 382.75)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 tmax,ss (total GB1211)

End point title	Part 2 tmax,ss (total GB1211) ^[11]
End point description:	
Time to reach maximum total plasma concentration at steady-state (on Day 21).	
End point type	Primary
End point timeframe:	
Time to maximum observed plasma concentration at steady-state (on Day 21).	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hour				
median (full range (min-max))	2.02 (1.00 to 12.00)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 tmax (total GB1211)

End point title	Part 2 tmax (total GB1211) ^[12]
End point description:	
Time to reach maximum total plasma concentration after drug administration.	
End point type	Primary
End point timeframe:	
Time to maximum observed plasma concentration.	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: hour				
median (full range (min-max))	4.00 (1.00 to 11.97)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 t_{1/2,ss} (total GB1211)

End point title	Part 2 t _{1/2,ss} (total GB1211) ^[13]
End point description:	
Terminal elimination half-life at steady-state.	
End point type	Primary
End point timeframe:	
Time until quantity reduce to half of its initial value at steady-state.	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: hour				
arithmetic mean (standard deviation)	9.37 (± 4.67)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 t_{1/2} (total GB1211)

End point title	Part 2 t _{1/2} (total GB1211) ^[14]
End point description:	
Terminal elimination half-life.	
End point type	Primary
End point timeframe:	
Time until quantity reduce to half of its initial value.	

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: hour				
median (full range (min-max))	20.72 (20.72 to 20.72)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 PTF (total GB1211)

End point title	Part 2 PTF (total GB1211) ^[15]
End point description:	Peak-trough fluctuation.
End point type	Primary
End point timeframe:	At steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percent				
arithmetic mean (standard deviation)	101.17 (\pm 58.36)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 RAC(Cmax) (total GB1211)

End point title	Part 2 RAC(Cmax) (total GB1211) ^[16]
End point description:	Accumulation ratio calculated on Day 21 using Cmax,ss.
End point type	Primary
End point timeframe:	From time 0 to the end of steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: NA				
arithmetic mean (standard deviation)	2.97 (\pm 1.03)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 RAC(AUC) (total GB1211)

End point title	Part 2 RAC(AUC) (total GB1211) ^[17]
End point description:	Accumulation ratio calculated on Day 21 using AUC(0- τ),ss.
End point type	Primary
End point timeframe:	From time 0 to the end of steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: NA				
arithmetic mean (standard deviation)	3.19 (\pm 1.10)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 AUC(0- τ),ss (unbound GB1211)

End point title	Part 2 AUC(0- τ),ss (unbound GB1211) ^[18]
End point description:	Area under the unbound plasma concentration versus time curve during a dosage interval tau at steady state.
End point type	Primary
End point timeframe:	From time 0 to dosage interval tau at steady state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: h.ng/mL				
arithmetic mean (standard deviation)	854.54 (\pm 500.65)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 AUC(0- τ) (unbound GB1211)

End point title	Part 2 AUC(0- τ) (unbound GB1211) ^[19]
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End point description:

Area under the unbound plasma concentration versus time curve during a dosage interval τ .

End point type	Primary
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End point timeframe:

From time 0 to dosage interval τ .

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: h.ng/mL				
arithmetic mean (standard deviation)	251.63 (\pm 132.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 C_{max,ss} (unbound GB1211)

End point title	Part 2 C _{max,ss} (unbound GB1211) ^[20]
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End point description:

Maximum measured unbound plasma drug concentration at steady-state (on Day 21).

End point type	Primary
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End point timeframe:

From time zero to t at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	89.11 (± 48.44)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cmax (unbound GB1211)

End point title	Part 2 Cmax (unbound GB1211) ^[21]
End point description:	Maximum measured unbound plasma drug concentration.
End point type	Primary
End point timeframe:	From time zero to t.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: ng/mL				
arithmetic mean (standard deviation)	28.62 (± 13.53)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cmin,ss (unbound GB1211)

End point title	Part 2 Cmin,ss (unbound GB1211) ^[22]
End point description:	Minimum measured unbound plasma drug concentration at steady-state (on Day 21).
End point type	Primary
End point timeframe:	From time zero to t at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	48.98 (\pm 29.72)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Cav,ss (unbound GB1211)

End point title	Part 2 Cav,ss (unbound GB1211) ^[23]
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End point description:

Average unbound plasma concentration at steady-state (on Day 21).

End point type	Primary
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End point timeframe:

At steady-state.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)	71.21 (\pm 41.72)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 tmax,ss (unbound GB1211)

End point title	Part 2 tmax,ss (unbound GB1211) ^[24]
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End point description:

Time to reach maximum unbound plasma concentration at steady-state (on Day 21).

End point type	Primary
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End point timeframe:

Time to maximum observed plasma concentration at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hour				
median (full range (min-max))	3.00 (2.92 to 3.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 tmax (unbound GB1211)

End point title	Part 2 tmax (unbound GB1211) ^[25]
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End point description:

Time to reach maximum unbound plasma concentration after drug administration.

End point type	Primary
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End point timeframe:

Time to maximum observed plasma concentration.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: hour				
median (full range (min-max))	3.00 (3.00 to 12.00)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Aet

End point title	Part 2 Aet ^[26]
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End point description:

Cumulative urinary excretion of the unchanged drug from administration during a dosage interval tau after single dosing.

End point type	Primary
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End point timeframe:

During a dosage interval τ after single dosing.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: mg				
arithmetic mean (standard deviation)	4.91 (\pm 3.34)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Fe

End point title	Part 2 Fe ^[27]
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End point description:

Fraction excreted into urine as unchanged drug after single dosing.

End point type	Primary
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End point timeframe:

From administration after single dosing.

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percent				
arithmetic mean (standard deviation)	4.91 (\pm 3.34)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Ae τ ,ss

End point title	Part 2 Ae τ ,ss ^[28]
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End point description:

Cumulative urinary excretion of unchanged drug from administration during a dosage interval τ at steady-state (on Day 21).

End point type	Primary
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End point timeframe:

From administration during a dosage interval τ at steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: mg				
arithmetic mean (standard deviation)	16.74 (± 10.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2 Fess

End point title	Part 2 Fess ^[29]
End point description:	Fraction excreted into urine as an unchanged drug at steady-state (on Day 21).
End point type	Primary
End point timeframe:	At steady-state (on Day 21).

Notes:

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

Justification: Descriptive statistics.

End point values	PK Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent				
arithmetic mean (standard deviation)	16.74 (± 10.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 AUClast (total GB1211)

End point title	Part 1 AUClast (total GB1211)
End point description:	Area under the total plasma concentration versus time curve from time 0 to the time of last quantifiable concentration (Tlast).
End point type	Primary
End point timeframe:	From time zero to the last quantifiable concentration t.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	8415.95 (± 5440.60)	6444.39 (± 3630.03)		

Statistical analyses

Statistical analysis title	ANOVA for AUClast
Comparison groups	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg) v Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	128.79
Confidence interval	
level	90 %
sides	2-sided
lower limit	74.89
upper limit	221.51

Primary: Part 1 AUCinf (total GB1211)

End point title	Part 1 AUCinf (total GB1211)
End point description:	
Area under the total plasma concentration versus time curve from time 0 to infinity.	
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	10949.80 (± 6001.70)	6679.97 (± 3734.07)		

Statistical analyses

Statistical analysis title	ANOVA for AUCinf
Comparison groups	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	156.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	72.32
upper limit	340.03

Primary: Part 1 Cmax (total GB1211)

End point title	Part 1 Cmax (total GB1211)
End point description:	Maximum measured total plasma drug concentration.
End point type	Primary
End point timeframe:	From time zero to t.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng/mL				

arithmetic mean (standard deviation)	587.40 (\pm 432.06)	621.89 (\pm 488.74)		
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Statistical analyses

Statistical analysis title	ANOVA for Cmax
Comparison groups	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	96.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	49.56
upper limit	187.27

Primary: Part 1 AUCextr (total GB1211)

End point title	Part 1 AUCextr (total GB1211) ^[30]
End point description:	Extrapolated area under the curve from the last quantifiable concentration to infinity as a percentage of AUCinf.
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: percent				
arithmetic mean (standard deviation)	7.38 (\pm 3.91)	3.66 (\pm 3.40)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 tmax (total GB1211)

End point title Part 1 tmax (total GB1211)^[31]

End point description:

Time to reach maximum total plasma concentration after drug administration.

End point type Primary

End point timeframe:

Time to maximum observed plasma concentration.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	3.49 (2.00 to 4.00)	3.00 (3.00 to 4.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 λz (total GB1211)

End point title Part 1 λz (total GB1211)^[32]

End point description:

First order terminal elimination rate.

End point type Primary

End point timeframe:

At terminal phase.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: h-1				

arithmetic mean (standard deviation)	0.03 (\pm 0.01)	0.04 (\pm 0.02)		
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Statistical analyses

No statistical analyses for this end point

Primary: Part 1 t_{1/2} (total GB1211)

End point title	Part 1 t _{1/2} (total GB1211) ^[33]
End point description: Terminal elimination half-life.	
End point type	Primary
End point timeframe: Time until quantity reduce to half of its initial value.	
Notes: [33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics.	

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: hour				
arithmetic mean (standard deviation)	35.03 (\pm 30.89)	17.21 (\pm 6.05)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 CL/F (total GB1211)

End point title	Part 1 CL/F (total GB1211) ^[34]
End point description: Apparent oral clearance.	
End point type	Primary
End point timeframe: From time 0 to infinity.	
Notes: [34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics.	

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: L/h				
arithmetic mean (standard deviation)	10.76 (± 4.05)	18.52 (± 8.15)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 Vz/F (total GB1211)

End point title	Part 1 Vz/F (total GB1211) ^[35]
End point description:	
Apparent volume of distribution.	
End point type	Primary
End point timeframe:	
From time 0 to infinity.	

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: litre(s)				
arithmetic mean (standard deviation)	343.24 (± 158.24)	449.90 (± 243.18)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 AUClast (unbound GB1211)

End point title	Part 1 AUClast (unbound GB1211)
End point description:	
Area under the total plasma concentration versus time curve from time 0 to the time of last quantifiable concentration (Tlast).	
End point type	Primary

End point timeframe:

From time zero to the last quantifiable concentration t.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	495.04 (± 303.87)	328.72 (± 157.15)		

Statistical analyses

Statistical analysis title	ANOVA for AUClast
Comparison groups	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg) v Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	144.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	87.99
upper limit	238.47

Primary: Part 1 AUCinf (unbound GB1211)

End point title	Part 1 AUCinf (unbound GB1211)
End point description:	Area under the total plasma concentration versus time curve from time 0 to infinity.
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	646.02 (± 319.48)	354.99 (± 159.35)		

Statistical analyses

Statistical analysis title	ANOVA for AUCinf
Comparison groups	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg) v Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	167.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	88
upper limit	319.85

Primary: Part 1 Cmax (unbound GB1211)

End point title	Part 1 Cmax (unbound GB1211)
End point description:	Maximum measured total plasma drug concentration.
End point type	Primary
End point timeframe:	From time zero to t.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng/mL				

arithmetic mean (standard deviation)	29.26 (\pm 18.01)	28.60 (\pm 19.56)		
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Statistical analyses

Statistical analysis title	ANOVA for Cmax
Comparison groups	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	102.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	57.31
upper limit	183.74

Primary: Part 1 AUCextr (unbound GB1211)

End point title	Part 1 AUCextr (unbound GB1211) ^[36]
End point description:	Extrapolated area under the curve from the last quantifiable concentration to infinity as a percentage of AUCinf.
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	
Notes:	[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: percent				
arithmetic mean (standard deviation)	8.04 (\pm 5.41)	8.28 (\pm 3.20)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 tmax (unbound GB1211)

End point title Part 1 tmax (unbound GB1211)^[37]

End point description:

Time to reach maximum total plasma concentration after drug administration.

End point type Primary

End point timeframe:

Time to maximum observed plasma concentration.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	3.50 (2.00 to 6.00)	3.00 (2.00 to 4.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 Rmax

End point title Part 1 Rmax^[38]

End point description:

Maximal rate of urinary excretion.

End point type Primary

End point timeframe:

From time zero to t.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: mg/h				

arithmetic mean (standard deviation)	0.55 (\pm 0.43)	0.56 (\pm 0.15)		
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Statistical analyses

No statistical analyses for this end point

Primary: Part 1 Ae(0-t)

End point title	Part 1 Ae(0-t) ^[39]
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End point description:

Cumulative urinary excretion of unchanged drug from administration until time t.

End point type	Primary
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End point timeframe:

From administration until time t.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: mg				
arithmetic mean (standard deviation)	9.59 (\pm 7.76)	7.84 (\pm 1.87)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 Fe

End point title	Part 1 Fe ^[40]
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End point description:

Fraction excreted into urine as unchanged drug after single dosing.

End point type	Primary
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End point timeframe:

From administration after single dosing.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percent				
arithmetic mean (standard deviation)	9.59 (\pm 7.76)	7.84 (\pm 1.87)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 ResAe

End point title	Part 1 ResAe ^[41]
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End point description:

Cumulative urinary excretion of unchanged drug from the time of the last quantifiable concentration (Tlast) to infinity, expressed as a percentage of total cumulative urinary excretion.

End point type	Primary
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End point timeframe:

From the time of the last quantifiable concentration (Tlast) to infinity.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: percent				
arithmetic mean (standard deviation)	9.04 (\pm 1.97)	1.19 (\pm 0.63)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 AUClast (total GB1211)

End point title	Part 3 AUClast (total GB1211)
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End point description:

Area under the total plasma concentration versus time curve from time 0 to the time of last quantifiable concentration (Tlast).

End point type	Primary
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End point timeframe:

From time zero to the last quantifiable concentration t.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	12477.52 (\pm 5659.07)	7566.33 (\pm 3096.46)		

Statistical analyses

Statistical analysis title	ANOVA for AUClast
Comparison groups	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg) v Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	159.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	100.14
upper limit	254.43

Primary: Part 3 AUCinf (total GB1211)

End point title	Part 3 AUCinf (total GB1211)
End point description:	
Area under the total plasma concentration versus time curve from time 0 to infinity.	
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	12424.07 (\pm 7303.42)	7892.42 (\pm 3157.95)		

Statistical analyses

Statistical analysis title	ANOVA for AUCinf
Comparison groups	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	161.59
Confidence interval	
level	90 %
sides	2-sided
lower limit	78.08
upper limit	334.43

Primary: Part 3 Cmax (total GB1211)

End point title	Part 3 Cmax (total GB1211)
End point description:	Maximum measured total plasma drug concentration.
End point type	Primary
End point timeframe:	From time zero to t.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng/mL				

arithmetic mean (standard deviation)	727.31 (\pm 355.34)	549.95 (\pm 330.67)		
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Statistical analyses

Statistical analysis title	ANOVA for Cmax
Comparison groups	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg) v Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	134.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	79.26
upper limit	228.22

Primary: Part 3 AUCextr (total GB1211)

End point title	Part 3 AUCextr (total GB1211) ^[42]
End point description:	Extrapolated area under the curve from the last quantifiable concentration to infinity as a percentage of AUCinf.
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	
Notes:	
	[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
	Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: percent				
arithmetic mean (standard deviation)	6.27 (\pm 5.13)	4.21 (\pm 2.39)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 tmax (total GB1211)

End point title | Part 3 tmax (total GB1211)^[43]

End point description:

Time to reach maximum total plasma concentration after drug administration.

End point type | Primary

End point timeframe:

Time to maximum observed plasma concentration.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
median (full range (min-max))	4.00 (2.00 to 6.00)	4.50 (2.00 to 6.02)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 λz (total GB1211)

End point title | Part 3 λz (total GB1211)^[44]

End point description:

First order terminal elimination rate.

End point type | Primary

End point timeframe:

At terminal phase.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h-1				

arithmetic mean (standard deviation)	0.04 (\pm 0.02)	0.04 (\pm 0.01)		
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Statistical analyses

No statistical analyses for this end point

Primary: Part 3 t_{1/2} (total GB1211)

End point title	Part 3 t _{1/2} (total GB1211) ^[45]
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End point description:

Terminal elimination half-life.

End point type	Primary
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End point timeframe:

Time until quantity reduce to half of its initial value.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hour				
arithmetic mean (standard deviation)	23.45 (\pm 11.82)	16.29 (\pm 2.49)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 CL/F (total GB1211)

End point title	Part 3 CL/F (total GB1211) ^[46]
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End point description:

Apparent oral clearance.

End point type	Primary
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End point timeframe:

From time 0 to infinity.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: L/h				
arithmetic mean (standard deviation)	10.50 (± 6.28)	14.28 (± 4.97)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 Vz/F (total GB1211)

End point title	Part 3 Vz/F (total GB1211) ^[47]
End point description:	
Apparent volume of distribution.	
End point type	Primary
End point timeframe:	
From time 0 to infinity.	

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: litre(s)				
arithmetic mean (standard deviation)	251.31 (± 161.95)	332.21 (± 105.92)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 AUClast (unbound GB1211)

End point title	Part 3 AUClast (unbound GB1211)
End point description:	
Area under the total plasma concentration versus time curve from time 0 to the time of last quantifiable concentration (Tlast).	
End point type	Primary

End point timeframe:

From time zero to the last quantifiable concentration t.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	746.15 (± 381.23)	439.19 (± 174.23)		

Statistical analyses

Statistical analysis title	ANOVA for AUClast
Comparison groups	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	162.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	99.55
upper limit	265.81

Primary: Part 3 AUCinf (unbound GB1211)

End point title	Part 3 AUCinf (unbound GB1211)
End point description:	
Area under the total plasma concentration versus time curve from time 0 to infinity.	
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: h.ng/mL				
arithmetic mean (standard deviation)	735.75 (± 505.43)	466.13 (± 173.82)		

Statistical analyses

Statistical analysis title	ANOVA for AUCinf
Comparison groups	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	165.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	80.8
upper limit	339.59

Primary: Part 3 Cmax (unbound GB1211)

End point title	Part 3 Cmax (unbound GB1211)
End point description:	Maximum measured total plasma drug concentration.
End point type	Primary
End point timeframe:	From time zero to t.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: ng/mL				

arithmetic mean (standard deviation)	34.41 (\pm 13.18)	28.08 (\pm 12.95)		
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Statistical analyses

Statistical analysis title	ANOVA for C _{max}
Comparison groups	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg) v Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Geometric mean Ratio (%)
Point estimate	111.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	69.9
upper limit	179.44

Primary: Part 3 AUC_{extr} (unbound GB1211)

End point title	Part 3 AUC _{extr} (unbound GB1211) ^[48]
End point description:	Extrapolated area under the curve from the last quantifiable concentration to infinity as a percentage of AUC _{inf} .
End point type	Primary
End point timeframe:	
Extrapolation to infinity.	
Notes:	
	[48] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
	Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: percent				
arithmetic mean (standard deviation)	6.57 (\pm 5.27)	6.55 (\pm 3.96)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 tmax (unbound GB1211)

End point title Part 3 tmax (unbound GB1211)^[49]

End point description:

Time to reach maximum total plasma concentration after drug administration.

End point type Primary

End point timeframe:

Time to maximum observed plasma concentration.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: hour				
median (full range (min-max))	3.00 (3.00 to 6.00)	3.00 (1.50 to 8.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 Rmax

End point title Part 3 Rmax^[50]

End point description:

Maximal rate of urinary excretion.

End point type Primary

End point timeframe:

From time zero to t.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: mg/h				

arithmetic mean (standard deviation)	0.16 (\pm 0.06)	0.22 (\pm 0.11)		
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Statistical analyses

No statistical analyses for this end point

Primary: Part 3 Ae(0-t)

End point title	Part 3 Ae(0-t) ^[51]
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End point description:

Cumulative urinary excretion of unchanged drug from administration until time t.

End point type	Primary
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End point timeframe:

From administration until time t.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: mg				
arithmetic mean (standard deviation)	3.13 (\pm 1.57)	4.72 (\pm 2.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 Fe

End point title	Part 3 Fe ^[52]
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End point description:

Fraction excreted into urine as unchanged drug after single dosing.

End point type	Primary
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End point timeframe:

From administration after single dosing.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percent				
arithmetic mean (standard deviation)	3.13 (\pm 1.57)	4.72 (\pm 2.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 3 ResAe

End point title	Part 3 ResAe ^[53]
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End point description:

Cumulative urinary excretion of unchanged drug from the time of the last quantifiable concentration (Tlast) to infinity, expressed as a percentage of total cumulative urinary excretion.

End point type	Primary
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End point timeframe:

From the time of the last quantifiable concentration (Tlast) to infinity.

Notes:

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

Justification: Descriptive statistics.

End point values	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: percent				
arithmetic mean (standard deviation)	5.19 (\pm 6.89)	4.00 (\pm 2.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 LiMAx test (mITT Population)

End point title	Part 2 LiMAx test (mITT Population)
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End point description:

Maximum liver function capacity assessment (the LiMAx® test is a dynamic liver function test based on the metabolism of 13C-methacetin by the liver-specific cytochrome P450 1A2 system).

End point type	Secondary
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End point timeframe:

Percent change from Baseline at Day 84.

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: percent				
arithmetic mean (standard deviation)	6.32 (± 39.30)	15.15 (± 36.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 LiMAx test (PP Population)

End point title	Part 2 LiMAx test (PP Population)
End point description: Maximum liver function capacity assessment (the LiMAx® test is a dynamic liver function test based on the metabolism of 13C-methacetin by the liver-specific cytochrome P450 1A2 system).	
End point type	Secondary
End point timeframe: Percent change from Baseline at Day 84.	

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: percent				
arithmetic mean (standard deviation)	4.43 (± 40.43)	15.15 (± 36.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan Liver stiffness (mITT Population)

End point title	Part 2 FibroScan Liver stiffness (mITT Population)
End point description: FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient elastography.	

End point type	Secondary
End point timeframe:	
Percent change from Baseline at Day 84.	

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: percent				
arithmetic mean (standard deviation)	-10.84 (± 66.26)	-21.42 (± 31.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan CAP (Liver steatosis) (mITT Population)

End point title	Part 2 FibroScan CAP (Liver steatosis) (mITT Population)
End point description: FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient elastography.	
End point type	Secondary
End point timeframe:	
Percent change from Baseline at Day 84.	

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: percent				
arithmetic mean (standard deviation)	-6.83 (± 14.24)	8.75 (± 31.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan Spleen Stiffness (mITT Population)

End point title	Part 2 FibroScan Spleen Stiffness (mITT Population)
End point description: FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient	

elastography.

End point type	Secondary
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End point timeframe:

Percent change from Baseline at Day 84.

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: percent				
arithmetic mean (standard deviation)	1.90 (± 30.25)	2.29 (± 35.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan Liver stiffness (PP Population)

End point title	Part 2 FibroScan Liver stiffness (PP Population)
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End point description:

FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient elastography.

End point type	Secondary
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End point timeframe:

Percent change from Baseline at Day 84.

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: percent				
arithmetic mean (standard deviation)	-10.00 (± 69.13)	-21.42 (± 31.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan CAP (Liver steatosis) (PP Population)

End point title	Part 2 FibroScan CAP (Liver steatosis) (PP Population)
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End point description:

FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient

elastography.

End point type	Secondary
End point timeframe:	
Percent change from Baseline at Day 84.	

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: percent				
arithmetic mean (standard deviation)	-6.48 (± 14.82)	8.75 (± 31.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2 FibroScan Liver stiffness (PP Population)

End point title	Part 2 FibroScan Liver stiffness (PP Population)
End point description:	
FibroScan®: Liver and spleen stiffness and liver steatosis measured by centrally-read transient elastography.	
End point type	Secondary
End point timeframe:	
Percent change from Baseline at Day 84.	

End point values	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: percent				
arithmetic mean (standard deviation)	-0.47 (± 30.31)	2.29 (± 35.27)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Screening until End of Study Visit

Adverse event reporting additional description:

The safety of the test product was assessed on the basis of clinical and laboratory examinations, local and general tolerability (vital signs, electrocardiogram (ECG), physical examination) and recording of all AEs and/or TEAEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Part 2 GB1211 100 mg (2 x 50 mg)
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Reporting group description: -

Reporting group title	Part 2 Placebo (2 x 0 mg)
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Reporting group description: -

Reporting group title	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
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Reporting group description: -

Reporting group title	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)
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Reporting group description: -

Reporting group title	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)
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Reporting group description: -

Reporting group title	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
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Reporting group description: -

Serious adverse events	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
ENCEPHALOPATHY			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMA HEPATIC			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
OESOPHAGEAL VARICES			
HAEMORRHAGE			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
ENCEPHALOPATHY			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMA HEPATIC			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
OESOPHAGEAL VARICES			
HAEMORRHAGE			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part 2 GB1211 100 mg (2 x 50 mg)	Part 2 Placebo (2 x 0 mg)	Part 1 Child-Pugh B Participants 100 mg GB1211 (2 x 50 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)	4 / 15 (26.67%)	0 / 6 (0.00%)
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Blood loss anemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hemoptysis			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 15 (6.67%) 1	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Azotemia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 15 (6.67%) 1	0 / 6 (0.00%) 0
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	0 / 6 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Part 1 Healthy Control 100 mg GB1211 (2 x 50 mg)	Part 3 Child-Pugh C Participants 100 mg GB1211 (2 x 50 mg)	Part 3 Healthy Control 100 mg GB1211 (2 x 50 mg)
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood sodium decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood urea increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
SARS-CoV-2 test positive			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood and lymphatic system disorders Blood loss anemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Hemoptysis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Azotemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Infections and infestations COVID-19			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2021	Main Exclusion Criteria: Have previously completed or withdrawn from a study investigating GB1211 and have previously received the investigational product was applicable for Parts 1 and 3 only, not for Part 2. On Day 1 the time of twelve-lead ECG measurement was changed from 4h (\pm 15 min) pre-dose to 4h (\pm 15 min) post-dose. The pregnancy test at the Screening Visit for all parts was amended. Urine pregnancy test was not performed, a serum pregnancy was completed. On day 21 and Day 63 (\pm 2 days): Clinical Laboratory testing Blood chemistry and hematology at pre-dose were not performed and the time of twelve-lead ECG measurement was changed from 4h (\pm 15 min) pre-dose to 4h (\pm 15 min) post-dose. In Section 13.1 Appendix 1, the Assigning a Child-Pugh score table was updated.
20 May 2022	The change was to indicate the samples for investigating the potential metabolites of GB1211. They were investigated using surplus plasma from GB1211 PK blood samples for all parts of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The objective was to assess GB1211 in subjects with hepatic impairment. Three months of exposure was sufficient to examine the safety, tolerability and PK parameters, but may not be sufficient for the clinical endpoints in the secondary objectives.

Notes: