



## Clinical trial results:

**An open-label, dose escalation, single-dose administration, multi-center phase I/II trial of FG001 (an imaging agent), in patients with glioblastoma scheduled for neurosurgery**

### Summary

EudraCT number	2020-003089-38
Trial protocol	DK SE
Global end of trial date	12 October 2023

### Results information

Result version number	v1 (current)
This version publication date	27 October 2024
First version publication date	27 October 2024

### Trial information

#### Trial identification

Sponsor protocol code	FG001-CT-001
-----------------------	--------------

#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	FluoGuide A/s
Sponsor organisation address	Ole Maaløes Vej 3, København N, Denmark, 2200
Public contact	Morten Albrechtsen, FluoGuide A/S, ma@fluoguide.com
Scientific contact	Morten Albrechtsen, FluoGuide A/S, ma@fluoguide.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	10 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2023
Global end of trial reached?	Yes
Global end of trial date	12 October 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Phase I:

1. To evaluate the safety and tolerability of single i.v. doses of FG001 in patients with malignant glioma scheduled for surgery
2. To establish the optimal dose for imaging of FG001 in patients with malignant glioma

Phase II:

1. To evaluate the efficacy of FG001 in patients with malignant glioma undergoing surgery and to compare it with the efficacy of 5-ALA in patients with malignant glioma undergoing surgery

Protection of trial subjects:

The trial patients were given ample time to consider participation in the trial before the consent was obtained. The informed consent documents were signed and dated by each patient and the Investigator, who had provided the information to the patient regarding the trial, before these patients had been exposed to any trial-related procedures, including screening tests for eligibility.

All patients received a copy of the patient information and the signed ICF. If new information potentially relevant to the trial patient's willingness to continue participation in the trial became available, a new patient information and ICF were provided to the IECs (and regulatory authorities, if required) for review and approval. The trial patients were informed about this new information and new consents were obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2020
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	Sweden: 5
Country: Number of subjects enrolled	Denmark: 59
Worldwide total number of subjects	64
EEA total number of subjects	64

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	40
From 65 to 84 years	24
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

During screening, eligible patients with the suspicion of the primary malignant glioma, as judged by MRI, were included in the trial. Each participant received a unique screening number which was entered in a screening log. At baseline visit an evaluation of their complete medical history, vital signs, etc. was performed.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

<b>Arm title</b>	Phase I
------------------	---------

Arm description:

Phase I was an open-label, non-randomized FiH phase with single-dose administration of FG001. It consisted of the dose escalation and dose elaboration parts, conducted at 1 site in Denmark. 40 patients were treated in Phase I, where all patients received both 5-ALA (as standard of care) and FG001.

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	
Other name	ICG-Glu-Glu-AE05
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The Investigational Medicinal Product (IMP) FG001 Drug Product i.v. (FG001 DP) was delivered in vials each vial containing 5.2 mg of freeze-dried FG001 for reconstitution with 5.0 ml of sterile water for injection (sWFI) before use. All patients received a single dose of reconstituted IMP through a slow i.v. injection lasting for up to 10 minutes.

In phase I, FG001 was administered i.v. in the morning on the day of the surgery (dose escalation) or in the evening the day before the surgery (dose elaboration).

Investigational medicinal product name	5-ALA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

A commercially available 5-ALA product for phases I and II (Gliolan® for oral administration) was purchased and supplied by the hospital. 5-ALA was administered in the morning, 2-4 hours before the surgery as an oral solution.

<b>Arm title</b>	Phase II - 5-ALA
------------------	------------------

Arm description:

In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. 5-ALA served as the active comparator to FG001, where patients were randomized to either FG001 or 5-ALA treatment.

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	5-ALA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

**Dosage and administration details:**

A commercially available 5-ALA product for phases I and II (Gliolan® for oral administration) was purchased and supplied by the hospital. 5-ALA was administered in the morning, 2-4 hours before the surgery as an oral solution.

<b>Arm title</b>	Phase II - FG001
------------------	------------------

**Arm description:**

In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. FG001 served as the experimental arm in Part II, where patients were randomized to either FG001 or 5-ALA treatment.

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	
Other name	ICG-Glu-Glu-AE05
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

**Dosage and administration details:**

The Investigational Medicinal Product (IMP) FG001 Drug Product i.v. (FG001 DP) was delivered in vials each vial containing 5.2 mg of freeze-dried FG001 for reconstitution with 5.0 m of sterile water for injection (sWfI) before use. All patients randomized to FG001 received a single dose of reconstituted IMP through a slow i.v. injection lasting for up to 10 minutes.

In phase II, FG001 was administered i.v. in the evening the day before the surgery. Patients received the planned dose of FG001 (36 mg per patient).

<b>Number of subjects in period 1</b>	Phase I	Phase II - 5-ALA	Phase II - FG001
Started	40	12	12
Completed	40	12	12

## Baseline characteristics

### Reporting groups

Reporting group title	Phase I
Reporting group description:	
Phase I was an open-label, non-randomized FiH phase with single-dose administration of FG001. It consisted of the dose escalation and dose elaboration parts, conducted at 1 site in Denmark. 40 patients were treated in Phase I, where all patients received both 5-ALA (as standard of care) and FG001.	
Reporting group title	Phase II - 5-ALA
Reporting group description:	
In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. 5-ALA served as the active comparator to FG001, where patients were randomized to either FG001 or 5-ALA treatment.	
Reporting group title	Phase II - FG001
Reporting group description:	
In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. FG001 served as the experimental arm in Part II, where patients were randomized to either FG001 or 5-ALA treatment.	

Reporting group values	Phase I	Phase II - 5-ALA	Phase II - FG001
Number of subjects	40	12	12
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	58.2	66.6	58.3
standard deviation	± 10	± 6.5	± 13.9
Gender categorical Units: Subjects			
Female	16	4	4
Male	24	8	8

Reporting group values	Total		
Number of subjects	64		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)	0 0 0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	24		
Male	40		

### Subject analysis sets

Subject analysis set title	Phase I: Escalation - Cohort 1 (1mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001: 1 mg	
Subject analysis set title	Phase I: Escalation - Cohort 2 (2mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 2mg	
Subject analysis set title	Phase I: Escalation - Cohort 3 (4mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 4mg	
Subject analysis set title	Phase I: Escalation - Cohort 4 (8mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 8mg	
Subject analysis set title	Phase I: Escalation - Cohort 5 (16mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 16 mg	
Subject analysis set title	Phase I: Escalation - Cohort 6 (24mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 24 mg	
Subject analysis set title	Phase I: Escalation - Cohort 7 (36mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 36 mg	
Subject analysis set title	Phase I: Escalation - Cohort 8 (48mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 48 mg	
Subject analysis set title	Phase I: Elaboration - Cohort 1 (16mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 16 mg

Subject analysis set title	Phase I: Elaboration - Cohort 2 (36mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 36 mg

Subject analysis set title	Phase I: Elaboration - Cohort 3 (48mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 48 mg

Reporting group values	Phase I: Escalation - Cohort 1 (1mg)	Phase I: Escalation - Cohort 2 (2mg)	Phase I: Escalation - Cohort 3 (4mg)
Number of subjects	3	3	3
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	66.3	60	60.3
standard deviation	± 9.8	± 5.1	± 8.1
Gender categorical Units: Subjects			
Female	3	1	1
Male	0	3	3

Reporting group values	Phase I: Escalation - Cohort 4 (8mg)	Phase I: Escalation - Cohort 5 (16mg)	Phase I: Escalation - Cohort 6 (24mg)
Number of subjects	4	3	3
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			

Age continuous Units: years arithmetic mean standard deviation	57.8 ± 7.5	49.0 ± 5.2	60.3 ± 9.5
Gender categorical Units: Subjects			
Female	2	1	1
Male	2	2	2

<b>Reporting group values</b>	Phase I: Escalation - Cohort 7 (36mg)	Phase I: Escalation - Cohort 8 (48mg)	Phase I: Elaboration - Cohort 1 (16mg)
Number of subjects	3	4	5
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	57.7 ± 13.3	60.5 ± 3.9	58.0 ± 8.5
Gender categorical Units: Subjects			
Female	1	3	1
Male	2	1	4

<b>Reporting group values</b>	Phase I: Elaboration - Cohort 2 (36mg)	Phase I: Elaboration - Cohort 3 (48mg)	
Number of subjects	5	4	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	62.6 ± 12.4	47.8 ± 10.7	

Gender categorical			
Units: Subjects			
Female	1	1	
Male	4	3	

---

## End points

### End points reporting groups

Reporting group title	Phase I
Reporting group description: Phase I was an open-label, non-randomized FiH phase with single-dose administration of FG001. It consisted of the dose escalation and dose elaboration parts, conducted at 1 site in Denmark. 40 patients were treated in Phase I, where all patients received both 5-ALA (as standard of care) and FG001.	
Reporting group title	Phase II - 5-ALA
Reporting group description: In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. 5-ALA served as the active comparator to FG001, where patients were randomized to either FG001 or 5-ALA treatment.	
Reporting group title	Phase II - FG001
Reporting group description: In Phase II, 24 patients were randomized to FG001 and 5-ALA arms. Randomization was performed after baseline assessments and before any trial treatment administration. FG001 served as the experimental arm in Part II, where patients were randomized to either FG001 or 5-ALA treatment.	
Subject analysis set title	Phase I: Escalation - Cohort 1 (1mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001: 1 mg	
Subject analysis set title	Phase I: Escalation - Cohort 2 (2mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 2mg	
Subject analysis set title	Phase I: Escalation - Cohort 3 (4mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 4mg	
Subject analysis set title	Phase I: Escalation - Cohort 4 (8mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 8mg	
Subject analysis set title	Phase I: Escalation - Cohort 5 (16mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 16 mg	
Subject analysis set title	Phase I: Escalation - Cohort 6 (24mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 24 mg	
Subject analysis set title	Phase I: Escalation - Cohort 7 (36mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 36 mg	
Subject analysis set title	Phase I: Escalation - Cohort 8 (48mg)
Subject analysis set type	Full analysis
Subject analysis set description: FG001 48 mg	
Subject analysis set title	Phase I: Elaboration - Cohort 1 (16mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 16 mg

Subject analysis set title	Phase I: Elaboration - Cohort 2 (36mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 36 mg

Subject analysis set title	Phase I: Elaboration - Cohort 3 (48mg)
Subject analysis set type	Full analysis

Subject analysis set description:

FG001 48 mg

### Primary: TBR (mean) values obtained with ORBEYE and ZEISS Pentero

End point title	TBR (mean) values obtained with ORBEYE and ZEISS Pentero <sup>[1]</sup>
-----------------	---

End point description:

The trial was descriptive in nature, and no confirmatory hypotheses were tested.

TBR = Tumor to Background Ratio.

End point type	Primary
----------------	---------

End point timeframe:

Duration of the Phase I part of the trial.

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: The trial was descriptive in nature, and no confirmatory hypotheses were tested.

End point values	Phase I: Escalation - Cohort 5 (16mg)	Phase I: Escalation - Cohort 6 (24mg)	Phase I: Escalation - Cohort 7 (36mg)	Phase I: Escalation - Cohort 8 (48mg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3 <sup>[2]</sup>	3 <sup>[3]</sup>	3 <sup>[4]</sup>	2 <sup>[5]</sup>
Units: TBR				
arithmetic mean (full range (min-max))				
ORBEYE	1.5 (1.3 to 1.7)	1.43 (1.2 to 1.7)	1.53 (1.4 to 1.6)	1.4 (1.4 to 1.4)
ZEISS	0 (0 to 0)	2.1 (2.1 to 2.1)	1.4 (1.4 to 1.4)	1.6 (1.5 to 1.7)

Notes:

[2] - n = 3 ORBEYE

[3] - n = 3 ORBEYE, n = 2 ZEISS

[4] - n = 3 ORBEYE, n = 1 ZEISS

[5] - n = 2 ORBEYE, n = 2 ZEISS

End point values	Phase I: Elaboration - Cohort 1 (16mg)	Phase I: Elaboration - Cohort 2 (36mg)	Phase I: Elaboration - Cohort 3 (48mg)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4 <sup>[6]</sup>	4 <sup>[7]</sup>	4 <sup>[8]</sup>	
Units: TBR				
arithmetic mean (full range (min-max))				
ORBEYE	1.5 (1.3 to 1.8)	1.9 (1.7 to 2.2)	1.4 (1.3 to 1.5)	
ZEISS	0 (0 to 0)	2.65 (1.9 to 3.7)	2.45 (2.2 to 2.8)	

Notes:

[6] - n = 4 ORBEYE

[7] - n = 4 ORBEYE, n = 4 ZEISS

[8] - n = 4 ORBEYE, n = 4 ZEISS

## Statistical analyses

No statistical analyses for this end point

### Primary: Indetermined or unexpected fluorescent tissue

End point title	Indetermined or unexpected fluorescent tissue <sup>[9]</sup> <sup>[10]</sup>
-----------------	--

End point description:

This endpoint corresponded to the occurrence of at least 1 indetermined or unexpected fluorescent tissue, where FG001- or 5-ALA-induced fluorescence was consistent with the histopathological assessment. This endpoint was assessed by calculating the proportion of patients with favorable outcome. The outcome was considered favorable if indetermined or unexpected fluorescence was observed in the EOS cavity and the subsequent histopathological assessment confirmed that biopsies taken from the fluorescent area of this cavity contained tumor cells.

End point type	Primary
----------------	---------

End point timeframe:

Duration of Phase II part of trial.

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: The trial was descriptive in nature, and no confirmatory hypotheses were tested.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results are provided for the sub-groups, where all sub groups belong to Phase I arm.

End point values	Phase II - 5-ALA	Phase II - FG001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Patients	12	12		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire duration of trial.

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

### Dictionary used

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

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

### Reporting groups

Reporting group title	Phase I cohorts
-----------------------	-----------------

Reporting group description: -

Reporting group title	Phase II cohorts
-----------------------	------------------

Reporting group description: -

Serious adverse events	Phase I cohorts	Phase II cohorts	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 40 (17.50%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Extradural haematoma			
subjects affected / exposed	1 / 40 (2.50%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 40 (2.50%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 40 (2.50%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	3 / 40 (7.50%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase I cohorts	Phase II cohorts	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)	24 / 24 (100.00%)	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	21 / 40 (52.50%)	9 / 24 (37.50%)	
occurrences (all)	21	9	
Electrocardiogram QT prolonged			
subjects affected / exposed	5 / 40 (12.50%)	0 / 24 (0.00%)	
occurrences (all)	5	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 40 (12.50%)	2 / 24 (8.33%)	
occurrences (all)	5	2	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 40 (10.00%)	3 / 24 (12.50%)	
occurrences (all)	4	3	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 40 (2.50%)	4 / 24 (16.67%)	
occurrences (all)	1	4	
Blood chloride decreased			
subjects affected / exposed	0 / 40 (0.00%)	3 / 24 (12.50%)	
occurrences (all)	0	3	
PCO2 increased			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	<p>3 / 24 (12.50%)</p> <p>3</p>	
<p>PO2 increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	<p>3 / 24 (12.50%)</p> <p>3</p>	
<p>Bilirubin conjugated increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	<p>2 / 24 (8.33%)</p> <p>2</p>	
<p>Blood lactic acid increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	<p>2 / 24 (8.33%)</p> <p>2</p>	
<p>Injury, poisoning and procedural complications</p> <p>Procedural headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>19 / 40 (47.50%)</p> <p>19</p>	<p>5 / 24 (20.83%)</p> <p>5</p>	
<p>Pneumocephalus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>11 / 40 (27.50%)</p> <p>11</p>	<p>7 / 24 (29.17%)</p> <p>7</p>	
<p>Incision site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 40 (0.00%)</p> <p>0</p>	<p>11 / 24 (45.83%)</p> <p>11</p>	
<p>Vascular disorders</p> <p>Hypertension</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 40 (7.50%)</p> <p>3</p>	<p>3 / 24 (12.50%)</p> <p>3</p>	
<p>Hypotension</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 40 (7.50%)</p> <p>3</p>	<p>1 / 24 (4.17%)</p> <p>1</p>	
<p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>11 / 40 (27.50%)</p> <p>11</p>	<p>3 / 24 (12.50%)</p> <p>3</p>	
<p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 40 (20.00%)</p> <p>8</p>	<p>0 / 24 (0.00%)</p> <p>0</p>	
<p>Hemianopia</p>			

subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3	0 / 24 (0.00%) 0	
Hemiparesis subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3	2 / 24 (8.33%) 2	
Aphasia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	1 / 24 (4.17%) 1	
Diplopia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 24 (0.00%) 0	
Dysaesthesia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 24 (0.00%) 0	
Nervous system disorder subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 24 (0.00%) 0	
Hemianopia homonymous subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	2 / 24 (8.33%) 2	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 9	3 / 24 (12.50%) 3	
Pyrexia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 24 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	2 / 24 (8.33%) 2	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	24 / 40 (60.00%) 24	2 / 24 (8.33%) 2	
Vomiting			

subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6	0 / 24 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	5 / 40 (12.50%) 5	0 / 24 (0.00%) 0	
Psychiatric disorders Adjustment disorder subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4	0 / 24 (0.00%) 0	
Confusional state subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	1 / 24 (4.17%) 1	
Hallucination, visual subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 24 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	2 / 24 (8.33%) 2	
Musculoskeletal and connective tissue disorders Pain in jaw subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6	2 / 24 (8.33%) 2	
Neck pain subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	2 / 24 (8.33%) 2	
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	28 / 40 (70.00%) 28	1 / 24 (4.17%) 1	
Hypoalbuminaemia subjects affected / exposed occurrences (all)	24 / 40 (60.00%) 24	13 / 24 (54.17%) 13	
Hypocalcaemia subjects affected / exposed occurrences (all)	14 / 40 (35.00%) 14	12 / 24 (50.00%) 12	
Hypermagnesaemia			

subjects affected / exposed	13 / 40 (32.50%)	1 / 24 (4.17%)
occurrences (all)	13	1
Hypophosphataemia		
subjects affected / exposed	8 / 40 (20.00%)	9 / 24 (37.50%)
occurrences (all)	8	9
Hypokalaemia		
subjects affected / exposed	6 / 40 (15.00%)	4 / 24 (16.67%)
occurrences (all)	6	4
Hyponatraemia		
subjects affected / exposed	3 / 40 (7.50%)	4 / 24 (16.67%)
occurrences (all)	3	4
Hyperkalaemia		
subjects affected / exposed	2 / 40 (5.00%)	5 / 24 (20.83%)
occurrences (all)	2	5
Hyperphosphataemia		
subjects affected / exposed	2 / 40 (5.00%)	0 / 24 (0.00%)
occurrences (all)	2	0
Acidosis		
subjects affected / exposed	0 / 40 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	2

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2020	Protocol version 2.0, amendment as response to GNA comments from the DKMA.
25 March 2021	Protocol version 3.0, amendment to include dose elaboration phase.
08 September 2021	Protocol version 4.0, amendment to include morning administration.
05 August 2022	Protocol version 5.1, amendment to move into Phase II of the trial.
18 January 2023	Protocol version 6.0, amendment to change the secondary objective of the trial.

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36416941>