



Clinical trial results:

An open-label, non-randomized, single dose, exploratory Phase II trial of FG001 (an imaging agent) for localization of biopsy-proven primary non-small cell lung cancer (NSCLC)

Summary

EudraCT number	2021-004389-37
Trial protocol	DK
Global end of trial date	02 June 2023

Results information

Result version number	v1 (current)
This version publication date	31 May 2024
First version publication date	31 May 2024

Trial information

Trial identification

Sponsor protocol code	FG001-CT-002
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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	Director Regulatory Affairs, FluoGuide A/S, alk@fluoguide.com
Scientific contact	Director Regulatory Affairs, FluoGuide A/S, alk@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	02 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2023
Global end of trial reached?	Yes
Global end of trial date	02 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate FG001 for the detection of NSCLC

Protection of trial subjects:

The trial was conducted, in compliance with the protocol, regulatory requirements, Good Clinical Practice (GCP) and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association. All subjects provided written informed consent to participate in the trial prior to being screened. All subjects received written and verbal information regarding the trial. The given information emphasized that participation in the trial was voluntary and that the subjects could withdraw from the trial at any time and for any reason. All subjects were given the opportunity to ask questions about the trial and were given sufficient time to decide whether to participate in the trial.

A subject was discontinued from the trial at any time if the subject, the Investigator, or the FluoGuide A/S evaluated that it was not in the subject's best interest to continue. The following were possible reasons for trial treatment discontinuation:

- Subject withdrawal of consent.
- Subject was not compliant with trial procedures.
- AE that in the opinion of the Investigator was in the best interest of the subject to discontinue trial participation.
- Protocol violation requiring discontinuation.
- Lost to follow-up.
- FluoGuide A/S request for early termination of trial.
- Subject death.

All subjects could withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. Reasonable attempts were made by the Investigator to provide a reason for the subject's withdrawal. The reason for the subject's withdrawal from the trial was specified in the subject's journal and the eCRF. If a subject was withdrawn from treatment due to an AE, the subject was followed and treated by the Investigator until the abnormal parameter or symptom has resolved or stabilized. Although subjects could withdraw from the trial at any time and for any reason, subject withdrawal was avoided to the extent possible.

Background therapy:

None

Evidence for comparator:

None

Actual start date of recruitment	24 May 2022
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	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	3
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at Copenhagen University Hospital, Rigshospitalet, Denmark. A total of 18 subjects were screened, 17 subjects received trial drug as a 36 mg single administration, 1 subject withdrew before dosing.

Pre-assignment

Screening details:

At the screening visit the subject's medical history and concomitant illnesses were obtained, and the previous and concomitant medication documented.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The trial was not blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

36 mg of FG001, administered day before surgery

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	FG001
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

36 mg of FG001, slow intravenous infusion

Arm title	Cohort 2
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Arm description:

36 mg of FG001, administered 2 days prior to surgery

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	FG001
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

36 mg of FG001, slow intravenous infusion

Number of subjects in period 1 ^[1]	Cohort 1	Cohort 2
Started	9	8
Completed	8	8
Not completed	1	0
Adverse event, serious fatal	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The disparity is due to 1 screening failure (withdrawal of consent) - a total of 18 subjects underwent screening, and a total of 17 subjects received trial drug (Cohort 1: N=9; Cohort 2: N=8). One subject in Cohort 1 died during the trial. This subject had a fatal TEAE of arterial rupture that was considered not related to the trial drug. 16 subjects completed the trial.

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	17	17	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	72		
full range (min-max)	58 to 83	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	8	8	
Fertility Status			
Units: Subjects			
Post-menopausal	9	9	
NA	8	8	
Ethnicity			
Units: Subjects			
White	17	17	
Tumor location			
Units: Subjects			
Peripheral	17	17	
Tumor size			
(cm, longest diameter)			
Units: centimetre			
arithmetic mean	3.84		
standard deviation	± 1.337	-	

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Full Analysis Set (FAS) or Intent-to-Treat Population: All subjects who were exposed to trial drug irrespective of their compliance to the planned course of treatment. All enrolled subjects dosed with FG001 and with any valid imaging information were included in the FAS.

Note: The FAS/ITT Population was removed from the analysis in a post database lock statistical analysis plan (SAP) addendum.

Subject analysis set title	Per-Protocol (PP) Set
Subject analysis set type	Per protocol

Subject analysis set description:

Per-Protocol (PP) Set: The set of FAS subjects who had at least 80% of the trial drug administered, and who did not have any major protocol violations that may affect the assessment of efficacy endpoints.

Note: The PP Set was redefined as a subset of the Safety Analysis Set in a post database lock SAP addendum.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety Analysis Set: All subjects who received trial drug.

Reporting group values	Full Analysis Set (FAS)	Per-Protocol (PP) Set	Safety Analysis Set
Number of subjects	17	17	17
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			
median	72	72	72
full range (min-max)	58 to 83	58 to 83	58 to 83
Gender categorical Units: Subjects			
Female	9	9	9
Male	8	8	8
Fertility Status Units: Subjects			
Post-menopausal	9	9	9
NA	8	8	8
Ethnicity Units: Subjects			
White	17	17	17
Tumor location Units: Subjects			
Peripheral	17	17	17

Tumor size			
(cm, longest diameter)			
Units: centimetre			
arithmetic mean	3.84	3.84	3.84
standard deviation	± 1.337	± 1.337	± 1.337

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: 36 mg of FG001, administered day before surgery	
Reporting group title	Cohort 2
Reporting group description: 36 mg of FG001, administered 2 days prior to surgery	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Full Analysis Set (FAS) or Intent-to-Treat Population: All subjects who were exposed to trial drug irrespective of their compliance to the planned course of treatment. All enrolled subjects dosed with FG001 and with any valid imaging information were included in the FAS. Note: The FAS/ITT Population was removed from the analysis in a post database lock statistical analysis plan (SAP) addendum.	
Subject analysis set title	Per-Protocol (PP) Set
Subject analysis set type	Per protocol
Subject analysis set description: Per-Protocol (PP) Set: The set of FAS subjects who had at least 80% of the trial drug administered, and who did not have any major protocol violations that may affect the assessment of efficacy endpoints. Note: The PP Set was redefined as a subset of the Safety Analysis Set in a post database lock SAP addendum.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: Safety Analysis Set: All subjects who received trial drug.	

Primary: Sensitivity for detection of NSCLC

End point title	Sensitivity for detection of NSCLC ^[1]
End point description: The primary efficacy endpoint (sensitivity measured as the proportion of biopsies encompassing active tumor tissue that were fluorescent and TBR values based on in vivo and ex vivo images) was challenging to achieve as the fluorescence signal was weak, resulting in mean TBR values between 1 and 2. Consequently, the surgeon could not be guided by the fluorescent light to sample the biopsies, and this is why these biopsies were not evaluated for fluorescence on the back table. A subjective evaluation of in vivo and ex vivo images was performed by the Sponsor team and identified that 11/15 subjects had a tumor that was fluorescent with FG001.	
End point type	Primary
End point timeframe: Duration 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 primary efficacy endpoint (sensitivity measured as the proportion of biopsies encompassing active tumor tissue that were fluorescent and TBR values based on in vivo and ex vivo images) was challenging to achieve as the fluorescence signal was weak. Subjective evaluation of in vivo and ex vivo images was performed by the Sponsor team and no statistical analyses were thus performed.	

End point values	Per-Protocol (PP) Set			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: tumours that were fluorescent with FG001	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Duration of the trial

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Safety Analysis Set
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Reporting group description:

Safety Analysis Set: All subjects who received trial drug.

All subjects in the Safety Analysis Set received a 36.0 mL administration of trial drug

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Vascular disorders			
Arterial rupture	Additional description: Arterial rupture and bleeding during surgery		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Hemothorax			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)		
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2022	Protocol Version 2.0: Removed "single site" wording throughout. Update to inclusion criterion 1 to include subjects with squamous-cell carcinoma. Update to inclusion criterion 3 to include subjects with tumor size ≥ 1.5 cm. Update the time window for PK sample collection at +44 hours post FG001 administration. Add new section describing financial aspects of the study including site payments.
23 November 2022	Protocol version 3.0: GCP statement was removed. Study visit structure updated to include an EoT visit at Day 4 from FG001 administration. Risk assessment information updated. Secondary efficacy endpoints were separated for Cohorts 1 and 2 and updated to include "Demonstrate exposure of FG001 after 1 hour and prior to surgery" for Cohort 2. Exploratory endpoint was updated to "To evaluate the correlation between the normalized FG001 intensities and the uPAR expression as determined by IHC". Exploratory endpoint was added "To explore the impact on normalized intensity level for surrounding benign tissue such as but not constrained to anthracosis and atelectasis". Correction to exclusion criterion 4. Planned number of subjects changed from "20 to 24" to "16 up to 44". Study design revised to allow up to 5 cohorts each including 8 subjects, with FG001 administration 2 days prior to surgery. Details of safety monitoring updated. PK sample timing updated, with an updated PK sampling schedule for Cohort 2. Vital signs timing updated. Sample size calculation updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported