



## Clinical trial results:

**An open-label, non-randomized, single center, single dose, exploratory phase II trial of FG001 (an imaging agent) for localization of oral and oropharyngeal squamous cell carcinoma**

### Summary

EudraCT number	2022-001361-12
Trial protocol	DK
Global end of trial date	11 July 2023

### Results information

Result version number	v1 (current)
This version publication date	29 March 2024
First version publication date	29 March 2024

### Trial information

#### Trial identification

Sponsor protocol code	FG001-CT-003
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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, Copenhagen, Denmark, DK-2200
Public contact	Andreas Kjær, MD, PhD, DMSc Chief Medical Officer, FluoGuide A/S, +45 3131 0844,
Scientific contact	Andreas Kjær, MD, PhD, DMSc Chief Medical Officer, FluoGuide A/S, +45 3131 0844,

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	03 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 July 2023
Global end of trial reached?	Yes
Global end of trial date	11 July 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 oral and oropharyngeal cancer

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	18 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Denmark: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

Notes:

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**Subjects enrolled per age group**

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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)	5
From 65 to 84 years	11
85 years and over	1

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at Copenhagen University Hospital, Rigshospitalet, Denmark. A total of 20 subjects were screened and 17 subjects were finally enrolled in the trial: four were included in the FG001 36 mg group, eight in the FG001 16 mg group and five in the FG001 4 mg group. One subject was withdrawn due to being inoperative.

### 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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	FG001 36 mg

Arm description:

Four subjects received FG001 at a dose of 36 mg.

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

The FG001 DP i.v. consisted of a vial containing 5.2 mg freeze-dried FG001 for reconstitution with sterile water for injection (sWfI) prior to use. All subjects received a single dose, slowly i.v. injection (up to 10 minutes) of the IMP (batch numbers: B4002507 and B4003582).

<b>Arm title</b>	FG001 16 mg
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Arm description:

Eight subjects received FG001 at a dose of 16 mg.

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

The FG001 DP i.v. consisted of a vial containing 5.2 mg freeze-dried FG001 for reconstitution with sterile water for injection (sWfI) prior to use. All subjects received a single dose, slowly i.v. injection (up to 10 minutes) of the IMP (batch numbers: B4002507 and B4003582).

<b>Arm title</b>	FG001 4 mg
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Arm description:

Five subjects received FG001 at a dose of 4 mg. One subject discontinued the trial by physician's

decision since the subject had no valid TBR imaging information.

Arm type	Experimental
Investigational medicinal product name	FG001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

The FG001 DP i.v. consisted of a vial containing 5.2 mg freeze-dried FG001 for reconstitution with sterile water for injection (sWfI) prior to use. All subjects received a single dose, slowly i.v. injection (up to 10 minutes) of the IMP (batch numbers: B4002507 and B4003582).

<b>Number of subjects in period 1</b>	FG001 36 mg	FG001 16 mg	FG001 4 mg
Started	4	8	5
Completed	4	8	4
Not completed	0	0	1
Physician decision	-	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	FG001 36 mg
Reporting group description: Four subjects received FG001 at a dose of 36 mg.	
Reporting group title	FG001 16 mg
Reporting group description: Eight subjects received FG001 at a dose of 16 mg.	
Reporting group title	FG001 4 mg
Reporting group description: Five subjects received FG001 at a dose of 4 mg. One subject discontinued the trial by physician's decision since the subject had no valid TBR imaging information.	

Reporting group values	FG001 36 mg	FG001 16 mg	FG001 4 mg
Number of subjects	4	8	5
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)	2	2	1
From 65-84 years	2	6	3
85 years and over	0	0	1
Age continuous Units: years			
arithmetic mean	59.0	69.4	69.0
standard deviation	± 21.0	± 12.1	± 16.5
Gender categorical Units: Subjects			
Female	1	3	4
Male	3	5	1

Reporting group values	Total		
Number of subjects	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)	5		
From 65-84 years	11		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	8		
Male	9		

## End points

### End points reporting groups

Reporting group title	FG001 36 mg
Reporting group description: Four subjects received FG001 at a dose of 36 mg.	
Reporting group title	FG001 16 mg
Reporting group description: Eight subjects received FG001 at a dose of 16 mg.	
Reporting group title	FG001 4 mg
Reporting group description: Five subjects received FG001 at a dose of 4 mg. One subject discontinued the trial by physician's decision since the subject had no valid TBR imaging information.	

### Primary: Sensitivity for Detection of Oral and Oropharyngeal Cancer Verified by Histology

End point title	Sensitivity for Detection of Oral and Oropharyngeal Cancer Verified by Histology <sup>[1]</sup>
End point description: The sensitivity was evaluated as the proportion of subjects with fluorescent tumors given the tumor had been histologically verified. The efficacy of FG001 (as a tumor imaging agent) was examined by the sensitivity, which was verified via the intensity of fluorescence from the specimen sampled. As per standard procedure at site the histopathological evaluation of a section of the tumor was performed.  A positive result was defined as correspondence between presence of cancer tissue in the biopsy sampled in an area with optical signal within the macroscopically visible tumor.	
End point type	Primary
End point timeframe: During surgery, punch biopsies were sampled to confirm sensitivity histopathologically.	
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: Not applicable.	

End point values	FG001 36 mg	FG001 16 mg	FG001 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	8	4	
Units: Subjects				
Subjects with a positive test result	4	8	4	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Tumor To Background Ratio (TBR): Signal intensity in tumor

End point title	Tumor To Background Ratio (TBR): Signal intensity in tumor
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**End point description:**

The optimal image for each subject was annotated for the tumor and three representative backgrounds (suspected healthy tissue). On the selected image, the tumor was annotated (delineated) based on the surgeon's knowledge of where the tumor was placed (including depth of tumor, as applicable). Hereafter, the areas of the anticipated healthy tissue were annotated as backgrounds. These were annotated as large areas near the tumor but anticipated not to be part of the tumor, both in vivo and ex vivo, for all subjects. An annotation tool was used for this and generated a pixel-based intensity value (range from 0-255). From the intensity values, a TBR was calculated.

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End point type	Secondary
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**End point timeframe:**

TBR was a secondary efficacy endpoint and was calculated as the fluorescence of the tumor relative to background tissue, as measured by NIR imaging. This was imaged in situ during resection.

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End point values	FG001 36 mg	FG001 16 mg	FG001 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	8	4	
Units: unit(s)				
median (inter-quartile range (Q1-Q3))				
Intensity Max (cancer)	159.82 (142.97 to 187.67)	157.07 (153.21 to 168.57)	169.77 (158.87 to 181.90)	
Intensity Mean (cancer)	122.68 (106.92 to 144.38)	114.50 (104.74 to 126.61)	114.08 (107.24 to 129.79)	
Intensity Background	52.35 (45.31 to 64.53)	56.36 (48.60 to 62.43)	53.54 (46.33 to 68.13)	
TBR Max value	3.08 (2.70 to 3.46)	2.94 (2.56 to 3.15)	3.26 (2.72 to 3.43)	
TBR Mean value	2.27 (2.18 to 2.44)	2.04 (1.91 to 2.18)	2.32 (1.90 to 2.37)	

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: PK profile determined by non-compartmental analysis**

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End point title	PK profile determined by non-compartmental analysis
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**End point description:**

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End point type	Secondary
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**End point timeframe:**

Samples were used to evaluate the PKs of FG001 and were taken at the following timepoints from administration of FG001: +1 Hour ( $\pm$  15 minutes), +13 hours ( $\pm$ 2 hours), +24 hours ( $\pm$  4 hours), +36 hours ( $\pm$  4 hours), and +44 hours ( $\pm$  6 hours).

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End point values	FG001 36 mg	FG001 16 mg	FG001 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 <sup>[2]</sup>	8 <sup>[3]</sup>	5 <sup>[4]</sup>	
Units: unit(s)				
arithmetic mean (standard deviation)				
Cmax (ng/mL)	8130 (± 1360)	4300 (± 1200)	577 (± 373)	
tmax (hr)	1.14 (± 0.0438)	1.08 (± 0.111)	3.38 (± 5.26)	
AUC0-inf (hr*ng/mL)	139000 (± 29600)	71300 (± 27400)	0 (± 0)	
AUC0-last (hr*ng/mL)	129000 (± 25500)	66300 (± 22800)	11400 (± 7270)	
t1/2 (hr)	11.2 (± 1.38)	12.3 (± 0.810)	0 (± 0)	

Notes:

[2] - N Cmax=4

N tmax=4

N AUC0-inf=4

N AUC0-last=4

N t1/2=4

[3] - N Cmax=8

N tmax=8

N AUC0-inf=7

N AUC0-last=8

N t1/2=7

[4] - N Cmax=5

N tmax=5

N AUC0-inf=0

N AUC0-last=3

N t1/2=0

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Safety was closely followed during the course of the trial.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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### Reporting groups

Reporting group title	FG001 36 mg
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Reporting group description:

Four subjects received FG001 at a dose of 36 mg.

Reporting group title	FG001 16 mg
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Reporting group description:

Eight subjects received FG001 at a dose of 16 mg.

Reporting group title	FG001 4 mg
-----------------------	------------

Reporting group description:

Five subjects received FG001 at a dose of 4 mg. One subject discontinued the trial by physician's decision since the subject had no valid TBR imaging information.

Serious adverse events	FG001 36 mg	FG001 16 mg	FG001 4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	FG001 36 mg	FG001 16 mg	FG001 4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	8 / 8 (100.00%)	4 / 5 (80.00%)
Investigations			
Blood bilirubin increased			
subjects affected / exposed	4 / 4 (100.00%)	2 / 8 (25.00%)	1 / 5 (20.00%)
occurrences (all)	4	2	1
General disorders and administration site conditions			
Hypothermia			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	1 / 8 (12.50%) 1	0 / 5 (0.00%) 0
Metabolism and nutrition disorders Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	5 / 8 (62.50%) 5	4 / 5 (80.00%) 4

**More information**

**Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2023	<p>This change was made to update the Interim Evaluation (IE).</p> <p>Description of changes:</p> <ul style="list-style-type: none"><li>• Inclusion of a dosing visit the day before surgery.</li><li>• Inclusion of the safety data as part of the IE meeting.</li><li>• Update of the IE.</li><li>• Inclusion of a new exclusion criterion (INR&lt;1.7).</li><li>• Correction of minor inconsistencies.</li></ul>

Notes:

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**Interruptions (globally)**

Were there any global interruptions to the trial? No

**Limitations and caveats**

None reported