# Clinical trial results:
# Phase II trial: uPAR-PET for prognostication in patients with non-small cell lung cancer

## Summary

| | |
|---|---|
| EudraCT number | 2015-005642-59 |
| Trial protocol | DK |
| Global end of trial date | 30 January 2025 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 May 2026 |
| First version publication date | 10 May 2026 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | AK-2015-LC-1 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Rigshospitalet |
| Sponsor organisation address | Blegdamsvej 9, Copenhagen, Denmark, 2100 |
| Public contact | Professor Andreas Kjær, Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet, 0045 35454011, akjaer@sund.ku.dk |
| Scientific contact | Professor Andreas Kjær, Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet, 0045 35454011, akjaer@sund.ku.dk |

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 | Interim |
| Date of interim/final analysis | 10 March 2026 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 January 2025 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 January 2025 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

68Ga-NOTA-AE105 PET/CT will be evaluated as a prognostic tool in patients with NSCLC by observer-blinded readings and compared to the prognostic performance of FDG-PET/CT and prognostic biomarkers as uPAR.

Protection of trial subjects:

It is emphasized that participation in the study is voluntary and will have no influence on the otherwise planned treatment, whether the patient will participate or not. The study is conducted in accordance with the Helsinki Declaration and the Good Clinical Practice (GCP). All clinical information about the participants is protected under the act on processing of Personal Data and the Danish Health Legislation. Overall, it is considered that the project is ethically sound, as there are no significant risks associated with the uPAR PET/CT imaging procedure.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 February 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Scientific research |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Denmark: 49 |
| Worldwide total number of subjects | 49 |
| EEA total number of subjects | 49 |

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) | 11 |
| From 65 to 84 years | 38 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Prospective inclusion of patients with non-small cell lung cancer.

### Pre-assignment

Screening details:

We prospectively screened 59 patients, whereof 49 were included. Four of the included patients did not undergo 68Ga-NOTA-AE105 PET/CT due to failed tracer production (n=3) and one patient did not show up for the PET/CT scan due to misunderstandings.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 49 |
| Number of subjects completed | 49 |

### Period 1

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

Blinding implementation details:

An experienced board-certified nuclear medicine physician analyzed the 68Ga-NOTA-AE105 PET/CT scans. If doubt regarding CT evaluation, a board-certified radiologist was consulted. The reader had access to previous imaging data, but was blinded to other patient data and follow-up data.

### Arms

| | |
|---|---|
| **Arm title** | Experimental arm |

Arm description:

All patients included for 68Ga-NOTA-AE105 PET/CT

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 68Ga-NOTA-AE105 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for concentrate for solution for infusion |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

Median dose of 198 MBq (range 176–203 MBq) i.v.

| **Number of subjects in period 1** | Experimental arm |
|---|---|
| Started | 49 |
| Not completed | 0 [1] |
| Completed | 49 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A total of 49 patients were included in the study. Of these, 45 patients underwent $^{68}$GaNOTAAE105 (uPAR) PET/CT. The four patients who did not undergo PET/CT were excluded due to failed tracer production (n = 3) or cancellation by the patient because of a misunderstanding (n = 1).

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall trial |
|---|---|

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 49 | 49 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 11 | 11 | |
| From 65-84 years | 38 | 38 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| median | 69 | | |
| full range (min-max) | 41 to 80 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 34 | 34 | |
| Male | 15 | 15 | |

### Subject analysis sets

| Subject analysis set title | Primary analysis set |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

All patients who underwent 68Ga-NOTA-AE105 PET/CT and had evaluable lesions visible on PET and/or CT.

| Subject analysis set title | Safety set |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The study population comprised all patients who were enrolled and underwent preoperative 68GaNOTAAE105 uPAR PET/CT imaging. A total of 45 patients were scanned and constitute the safety and feasibility analysis set (primary analysis set).

| Reporting group values | Primary analysis set | Safety set | |
|---|---|---|---|
| Number of subjects | 45 | 45 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |

| | | | |
|---|---|---|---|
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 10 | 10 | |
| From 65-84 years | 35 | 35 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 69 | 69 | |
| full range (min-max) | 41 to 80 | 41 to 80 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 26 | 31 | |
| Male | 11 | 14 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Experimental arm |
| Reporting group description: All patients included for 68Ga-NOTA-AE105 PET/CT | |
| Subject analysis set title | Primary analysis set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All patients who underwent 68Ga-NOTA-AE105 PET/CT and had evaluable lesions visible on PET and/or CT. | |
| Subject analysis set title | Safety set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The study population comprised all patients who were enrolled and underwent preoperative 68GaNOTAAE105 uPAR PET/CT imaging. A total of 45 patients were scanned and constitute the safety and feasibility analysis set (primary analysis set). | |

### Primary: Feasibility of uPAR PET

| | |
|---|---|
| End point title | Feasibility of uPAR PET[1] |
| End point description: Feasibility was defined as successful completion of the uPAR PET/CT scan with evaluable imaging data suitable for quantitative analysis. | |
| End point type | Primary |
| End point timeframe: From tracer administration to completion of the planned uPAR PET/CT examination. | |

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: This primary endpoint is descriptive. Feasibility was assessed as the proportion of included patients who successfully underwent uPAR PET imaging. Of 49 included patients, 45 completed the PET/CT examination; the remaining four were due to failed tracer production (n=3) and patient cancellation (n=1). Tracer uptake was observed in all imaged tumors. As no inferential analysis was planned, no statistical analysis was applicable.

| End point values | Primary analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 45 | | | |
| Units: Number of patients | | | | |
| Completion | 45 | | | |
| Non completion | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Safety

| | |
|---|---|
| End point title | Safety[2] |
| End point description: Safety was assessed by recording adverse events related to administration of the investigational tracer, | |

including serious adverse events and suspected unexpected serious adverse reactions.

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

End point timeframe:

From administration of $^{8}$GaNOTAAE105 until 24 hours after tracer injection.

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: This primary endpoint is descriptive in nature. Safety was assessed by recording the occurrence of adverse events following administration of the PET tracer. No tracerrelated adverse events were observed in the study population. As no events occurred, no formal statistical analysis was applicable or performed.

| **End point values** | Safety set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 45 | | | |
| Units: Number of subjects | | | | |
| No adverse events | 45 | | | |
| Adverse events | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

Within 24 hours of 68Ga-NOTA-AE105 injection

Adverse event reporting additional description:

The study was initiated before the publication of CTCAE version 5.0; therefore, adverse events were assessed using CTCAE version 4.0

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

### Dictionary used

| | |
|---|---|
| Dictionary name | CTCAE |
| Dictionary version | 4 |

### Reporting groups

| | |
|---|---|
| Reporting group title | All patients scanned |

Reporting group description: -

| **Serious adverse events** | All patients scanned | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | All patients scanned | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No nonserious adverse events were reported in this study. The 68GaNOTAAE105 tracer has a short physical halflife, and safety monitoring was therefore focused on the period during and immediately after tracer administration and the uPAR PET/CT procedure. Adverse events were actively monitored and recorded within the first 24 hours following tracer administration. No adverse events considered related to the tracer or imaging procedure were observed during this period.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 23 January 2023 | A total of four amendments have submitted, Amendment 3 and 4 (change in inclusion criteria and study population) qualifies as substantial amendments. The remaining amendments were nonsubstantial, as they did not impact participant safety, study design, or scientific validity.<br>In Amendment 3 (23-JAN-2023), the inclusion criteria were amended to include only local (operable) NSCLC and LCNEC (pilot study), as recruitment of patients with metastatic NSCLC proved challenging and the study was no longer considered relevant in mesothelioma due to developments in treatment. |
| 10 April 2024 | A total of four amendments have submitted, Amendment 3 and 4 (change in inclusion criteria and study population) qualifies as substantial amendments. The remaining amendments were nonsubstantial, as they did not impact participant safety, study design, or scientific validity.<br>In Amendment 4 (10-APR-2024), the inclusion criteria were narrowed to include only patients with operable NSCLC, as patients with LCNEC have been included in a separate, parallel study. A pilot study in patients with LCNEC was therefore not expected to provide additional knowledge on this PET tracer. The last patient is included by the end of 2024, and an extension of the approval period has therefore been requested. All patients are intended to be followed for five years, and the final review of medical records will therefore take place before December 31st 2029. As the followup consists solely of medical record review and no trialrelated procedures, the study has, by agreement with the GCP unit, not been transferred to CTIS.<br>In Amendment 4 the sample size was reduced to 61 patients.<br>The final analysis will include fewer patients than originally planned due to interrupted recruitment and availability of complete paired imaging and tissue data. However, a subset of patients was enrolled early (2016-2017) and has substantially longer followup than planned, resulting in mature timetoevent data. As the study was designed as a survival analysis with an assumed large effect size, extended followup partially compensates for the reduced sample size. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 01 January 2018 | Because of capacity constraints, staff shortages, slow accrual in advanced/unresectable disease and COVID, the inclusion was paused from 2018-2022. | 01 February 2023 |

Notes:

### Limitations and caveats

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

This submission represents an interim analysis. The primary endpoint OS and secondary endpoint DFS have not yet been reached due to limited follow-up time. Final analyses will be reported once sufficient follow-up time has been achieved.

Notes: