ISRCTN18425518 https://doi.org/10.1186/ISRCTN18425518

The assessment of D5 Ethanol as a marker in exhaled breath to distinguish between people with and without lung cancer

Submission date 23/02/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 11/08/2023	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 13/06/2025	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Despite decades of research, lung cancer has one of the lowest survival rates of all cancers. The study team hope that this trial will contribute towards a breath-based screening programme for lung cancer, which will lead to earlier detection and higher survival rates. Recent research has shown that cells inside the body produce substances that end up in the lungs and are breathed out, or 'exhaled'. These studies have shown that those substances may be different if someone is suffering from particular diseases, including cancer. Research has also shown that if a certain product ("probe") is administered, it may be processed differently in your body if you are healthy, compared to if you have a disease. This study aims to see if people with cancer can be distinguished from people without lung cancer by collecting and analysing their breath after having received an intravenous infusion of probe D5-ethyl- ßD-glucuronide (OWL-EVO1). Ethyl glucuronide is a substance that is already naturally produced in your body in much larger amounts if you consume alcohol. For this study the ethyl molecule has been labelled (which is why it's called D5-ethyl), which means a marker has been attached to it, allowing it to be easily recognized on your breath. This label is not radioactive, and labelling is a harmless approach commonly used in research. When the probe is broken down in your body you will partly exhale it as a very small amount of alcohol. The other part of the molecule (glucuronic acid) will be removed from your blood by your kidneys. The amount of alcohol that is expected to be released in your blood will be less than when you would drink 1ml of wine.

Who can participate?
Subjects aged between 45-85, who have had a CT as part of clinical care, showing either the presence or absence of lung cancer may be eligible to take part in the study.

What does the study involve?
The study will be run at NHS sites and will involve 1 dose of OWL-EVO1 and multiple breath samples (that will last between 5-15 mins each).

What are the possible benefits and risks of participating?
Benefits:

You will not directly benefit from taking part in this research. We hope that the information we obtain from the study will help us to develop a breath test that can help diagnose cancer at an earlier stage
in the future.
Risks:
*There will be one blood test and the probe will be administered via a small tube (catheter) into the vein. This infusion will be done by trained and experienced members of the study team however, some people may experience some bruising around the area where the skin is pierced.
*Patients will be asked to breathe into a face mask or mouthpiece for 5-15 minutes. This procedure will not interfere with the patient's normal breathing pattern. However, some patients might feel somewhat uncomfortable breathing for a longer period into a face mask.
* OWL-EVO1 has been administered in Phase 1 a and 1 b studies to 39 subjects. No serious adverse events were recorded. OWL-EVO1's scientific naming is D5-ethyl- ßD-glucuronide; ethyl glucuronide is a substance that is already naturally produced in the human body when consuming alcohol. However, administering the probe does not have the same effect as consuming alcohol because the probe is a minor metabolite of alcohol that does not have the same effects alcohol is known for. For the purpose of this study the ethyl molecule has been labelled (= D5-ethyl). This label is non-radioactive, and labelling with D5 is a harmless labelling approach commonly used in research.
*Participants will be continuously monitored during probe administration and for up to on 3 hours after receiving the probe. Adverse event monitoring will be conducted and participants will receive a follow-up phone call 3-5 days after taking part in the study.
* During the study visit day when the probe is administered, subjects are expected to remain at the site for approximately 4-5 hours. Subjects will be well informed of the expected time investment for the study so that they can assess whether they can make this time investment. Time and travel expenses for the visit will be compensated. The visits will be scheduled in agreement with the subjects to ensure they can take place on a day that is feasible for the participant.
* Data protection: All the information that is collected about the subjects for this study will be kept strictly confidential.

Where is the study run from?
Owlstone Medical Limited (UK)

When is the study starting and how long is it expected to run for?
February 2023 to June 2025

Who is funding the study?
Owlstone Medical Limited (UK)

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-004433-20

Integrated Research Application System (IRAS)
1007323

ClinicalTrials.gov (NCT)
NCT06193239

Protocol serial number
OML-EV2, IRAS 1007323

Study information

Scientific Title
Diagnostic accuracy study for OWL-EVO1 as a lung cancer EVOC® probe

Acronym
Evolution 2

Study objectives
1. Diagnostic accuracy: To assess the diagnostic accuracy of the OWL-EVO1 Breath Biopsy test to differentiate between individuals with representative relevant clinical presentations in which

the test is intended to be used (lung cancer and controls contrast groups representing clinical presentation that include lung cancer as part of its differential diagnosis).
In this context relevant clinical presentations means:
• Individuals eligible for lung cancer screening based on low dose CT with or without lung cancer.
• Incidental findings on CT-scan suspicious of lung cancer
• Clinical presentations which include lung cancer as part of their differential diagnosis
2. Optimised test: Define a test protocol that achieves the optimal balance between minimising healthcare worker effort, maximising tolerability, and optimising diagnostic accuracy for the intended use setting.
3. Safety and tolerability of OWL-EVO1

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 30/08/2023, East of England - Cambridge Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8096; cambridgeeast.rec@hra.nhs.uk), ref: 23/EE/0066

Study design
Interventional study

Primary study design
Interventional

Study type(s)
Diagnostic, Safety

Health condition(s) or problem(s) studied
Lung cancer

Interventions
Group 1: Lung cancer patient – administered the OWL-EVO1 probe at a maximum dose of 2mg /kg intravenously. The patients will be administered one dose of the probe on the first study day and may be called back for an optional visit 1 week to 6 months later to repeat the initial study day and receive an additional dose of the probe.
Group 2: Control (Contrast group) - administered the OWL-EVO1 probe at a maximum dose of 2mg/kg intravenously. The patients will be administered one dose of the probe on the first study day and may be called back for an optional visit 1 week to 6 months later to repeat the initial study day and receive an additional dose of the probe.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Ethyl-β-D-glucuronide-(ethyl-d5)

Primary outcome(s)

The diagnostic accuracy of OWL-EVO1 to distinguish between those with lung and without lung cancer on breath measured using breath samples taken on Day 1 pre- and post-infusion, reported using a Receiver Operator Characteristic Curve, NPV, PPV, Sensitivity, Specificity & Likelihood Ratios. Metrics will be reported for overall test performance as well as pre-defined subgroup analyses.

Key secondary outcome(s))
1. Optimised test: Locked down protocol for breath sampling (method, timing, posture and duration) and OWL-EVO1 dose at Day 1 pre and post infusion breath samples
2. Safety and tolerability: Refined understanding of safety and tolerability of OWL-EVO1 based on reported Adverse Events associated with probe administration. AEs assessed on Day 1 and phone call between day 3 and 5 post infusion

Completion date
30/06/2025

Eligibility

Key inclusion criteria
1. Aged 45-85 years
2. Ability to provide informed consent
3. Receiving a thoracic CT

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
45 years

Upper age limit
85 years

Sex
All

Total final enrolment
187

Key exclusion criteria
1. Anticipated inability to complete the breath sampling procedure (e.g., inability to maintain adequate ventilation unaided or claustrophobia).
2. Received an investigational medical product in the context of a Clinical Trial (CTIMP) during the 28 days prior to administration of the (first) probe.
3. Individuals under diagnostic investigation for a potential malignancy other than lung cancer

that has not yet reached a conclusive diagnosis*.
4. Individuals with an inconclusive lung abnormality (indeterminate pulmonary nodule) on CT-scan requiring CT-based monitoring rather than biopsy and/or treatment.
5. Documented history of pulmonary surgery or endobronchial interventional procedures other than biopsy, lavage, or bronchial brushings. These include surgical resection, Video Assisted Thoracic Surgery (VATS), bronchial thermoplasty and coiling, airway stenting or other interventional bronchoscopic procedures.
6. Pregnant or breastfeeding women and women of child-bearing potential not using adequate contraceptive methods.
7. Individuals under investigation for suspicion of lung cancer who are unlikely to receive a definitive tissue diagnosis of lung cancer prior to treatment (e.g. stereotactic ablative radiotherapy without tissue confirmation).
*Note; Individuals with a confirmed cancer diagnosis ARE eligible (such as a diagnosis of prostate cancer now undergoing hormone therapy). Individuals scheduled to attend a cancer screening program; prostate, breast, lung, colon, ARE eligible.

Date of first enrolment
01/09/2023

Date of final enrolment
31/05/2025

Locations

Countries of recruitment
England

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Owlstone Medical Limited

Funder(s)

Funder type
Industry

Funder Name
Owlstone Medical Limited

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as plans for data sharing were not included in the IRAS form, and so there will not be ethical approval for this. This will be reviewed by Owlstone Medical at a later date.

IPD sharing plan summary
Not expected to be made available