ISRCTN11063656 https://doi.org/10.1186/ISRCTN11063656

# Identifying new tumour markers in oesophageal (gullet) and gastroesophageal (stomach/gullet) cancers

| | | |
|---|---|---|
| **Submission date**<br>12/08/2022 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[X] Results<br>[_] Individual participant data |
| **Registration date**<br>19/08/2022 | **Overall study status**<br>Completed | |
| **Last Edited**<br>28/03/2025 | **Condition category**<br>Cancer | |

## Plain English summary of protocol

Background and study aims
People with oesophageal (gullet) and gastroesophageal (stomach/gullet) cancers receive treatments such as, chemotherapy, radiotherapy and surgery, but often they are not effective in curing the cancer. Scientists and doctors are working together to make develop new immunotherapy treatments, immunotherapy helps the immune system fight cancer. There are some immunotherapy treatments for oesophageal and gastroesophageal cancers, but they only work in a small number of people.
There are markers in the cancer cells which can sometimes tell which immunotherapy will work best for a person, called neoantigens. To be able to develop more immunotherapy treatments we first have to find out which neoantigens are in oesophageal and gastroesophageal cancers. This study will collect cancer tissue samples from people with oesophageal and gastroesophageal cancer. Scientists at Platinum Informatics Ltd will look at the cancer tissue to identify neoantigens.

Who can participate?
• 18 years of age or older
• Willing and able to provide written informed consent
• Histologically confirmed oesophageal or gastroesophageal junctional adenocarcinoma.

What does the study involve?
Participants will be asked to provide tissue biopsy samples of their gullet or gullet/stomach cancer tumours. These samples will be taken when participants are already having procedures carried out for their medical care for their cancer. A small number of participants may be asked if they agree to having an endoscopy specifically to collect biopsy samples for the research study if they are not due to have a medical care procedure. Participants will also give a blood sample when their tissue biopsy sample is collected and 18 weeks later. Participants will be followed up for 18 weeks where details of how their condition progresses will be collected. Participants may also have optional biopsy samples taken on 3 more occasions and optional blood samples on 2 more occasions during the 18 week follow-up period. These will be taken if a participant is having a medical care procedure which would allow this.

What are the possible benefits and risks of participating?
The trial may not immediately benefit the participant, but if the the trial may identify new neoantigens which may lead to targeting of treatments for this group of participants.
Risks:
The tissue biopsy samples will be collected wherever possible when the participants are undergoing biopsy
procedures as part of their routine care. If that is not possible, then the biopsies will be carried out for the study
purpose only. Collecting these tissue samples is considered safe, but the possible risks include:
- Bleeding at the time the samples are removed.
- Infection at the site where the samples are removed.
- Pain at the time the samples are removed.
These complications happen 1 in 1000 endoscopic biopsies and are usually minor and short-lived (discomfort or
minor bleeding at biopsy sites).

Where is the study run from?
University of Dundee (UK)

When is the study starting and how long is it expected to run for?
December 2021 to November 2023

Who is funding the study?
Platinum Informatics Ltd (UK)

Who is the main contact?
Russell Petty, r.petty@dundee.ac.uk

# Contact information

### Type(s)
Scientific, Principal investigator

### Contact name
Prof Russell Petty

### ORCID ID
https://orcid.org/0000-0003-2055-4572

### Contact details
TASC
Level 3 Residency block
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY
+44 1382 383423
r.petty@dundee.ac.uk

### Type(s)
Public

**Contact name**
Mrs Margaret Band

**Contact details**
Tayside Clinical Trials Unit
TASC
Level 3, Residency Block
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY
+44 1382 383097
m.band@dundee.ac.uk

# Additional identifiers

**Integrated Research Application System (IRAS)**
309452

**Protocol serial number**
2-014-22

# Study information

**Scientific Title**
Proteomic Profiling of Oesophageal Adenocarcinoma Neoantigens

**Acronym**
PROTEAN

**Study objectives**
To characterise neoantigen profiles of oesophageal or gastroesophageal junction adenocarcinomas

**Ethics approval required**
Old ethics approval format

**Ethics approval(s)**
Approved 24/08/2022, Wales REC 6 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK: +44 2920 230457; Wales.REC6@wales.nhs.uk), ref: 22/WA/0223

**Primary study design**
Observational

**Study design**
Observational study with specimen collection

**Study type(s)**

Screening

## Health condition(s) or problem(s) studied
Oesophageal cancer

## Interventions
Medical history
• To confirm eligibility
• Location of primary tumour
• Histological and molecular diagnosis details – Human epidermal growth factor receptor 2 (HER2), PD-L1 testing
• Tumour stage according to AJCC/UICC version 8 for cancers of the oesophagus and stomach
• Stage and location of metastases
• Progression assessment – RECIST Criteria 1.1
• Medical co-morbidities
• Smoking history

Demographics
• Age, gender, body mass index

Concomitant medication
• Details of any scheduled or prior cancer treatment

Biopsy
• A fresh tumour biopsy will be collected:
o Prior to the commencement of any subsequent scheduled anticancer treatments*; OR
o After the completion of the latest line of anticancer treatment*; OR
o During follow up when a participant is not receiving or is between scheduled anti-cancer treatments*.
*Anti-cancer treatments excluding surgery
• The biopsy may be obtained from any site of tumour, primary or metastatic as considered the most appropriate and feasible at the time of the procedure.
• Biopsies from more than one tumour site may be obtained at the same time point and procedure, but this is not mandatory, only biopsy of a single tumour site is required for study participation.
• Up to 10 biopsies, approximately 2mm each, will be taken at each timepoint and if tumour biopsy is being undertaken by endoscopy 2 biopsies approximately 2mm each of adjacent normal oesophageal or gastric mucosa.
• As far as possible, tumour biopsies for the study will be obtained during routine clinical care procedures e.g. endoscopy, surgery, stenting. However, where this is not possible, consent will be requested for study specific procedures for biopsy to obtain tumour material.
• Participants may provide additional consent for further biopsies during further routine clinical care procedures to be taken as an optional part of the study.

Research bloods
• A maximum of 20ml of blood will be collected at each visit.
• Sites which have the facilities to carry out peripheral blood mononuclear cell preparations (PBMC) analysis will process and complete analysis on site. These samples will be processed at sites for PBMCs.
• Details of sample collection, processing, storage and transfer will be provided in PROTEAN Clinical Sample Handling Manual.

Outcome assessment
• Tumour response status according to RECIST v1.1
• Overall Survival
• Adverse events (AE)

The total duration of observation and follow up is 18 weeks.

### Intervention Type
Other

### Primary outcome(s)
Neoantigen profiles for individual patients with oesophageal or gastroesophageal junction adenocarcinomas measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) of tumour biopsies taken at Day 1 and a maximum of 3 further optional research biopsy samples may be collected between day 1 and week 18, timings will vary for participants for these biopsies to fit in with their standard care procedures.

### Key secondary outcome(s)
1. Proportion of patients in which neoantigen profiles are successfully generated measured as percent of patients in the study for whom neoantigen profiles are obtained by liquid chromatography-tandem mass spectrometry (LC-MS/MS) of their tumour biopsies taken at Day 1 and a maximum of 3 further optional research biopsy samples may be collected between day 1 and week 18, timings will vary for participants for these biopsies to fit in with their standard care procedures.
2. Characterise pre-existing T cell responses to identified neoantigens measured by ex vivo IFN Gamma ELISPOT assays on peripheral blood mononuclear cells isolated from patients stimulated with synthesized neoepitope peptides identified from patient's tumour biopsies
3. Correlate objective response rate, disease control rate, progression free survival and overall survival with neoantigen profiles measured by analysis of participants grouped by any identified common features of neoantigen profiles of tumours
4. Genomic and transcriptomic analysis and neoantigen validation measured by Whole genome sequencing and RNA sequencing of tumour biopsies and compared to neoantigen profiles of individual patients with oesophageal or gastroesophageal junction adenocarcinomas measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) of tumour biopsies

### Completion date
11/10/2023

## Eligibility

### Key inclusion criteria
1. 18 years of age or older
2. Willing and able to provide written informed consent
3. Histologically confirmed oesophageal or gastroesophageal junctional adenocarcinoma.
4. Able to provide a tumour biopsy sample as per protocol requirements

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 Years

### Sex
All

### Total final enrolment
86

### Key exclusion criteria
1. Concurrent systemic anti-cancer treatment and/or radiotherapy (participants undergoing cancer surgery are eligible.)
2. Any significant medical condition that in the opinion of the Principal Investigator (PI) would impair the ability of the participant to complete the requirements of the protocol

### Date of first enrolment
01/09/2022

### Date of final enrolment
31/03/2023

## Locations

### Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

### Study participating centre
**Ninewells Hospital**
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

### Study participating centre

**Glasgow Royal Infirmary**
84 Castle Street
Glasgow
United Kingdom
G4 0SF

**Study participating centre**
**University Hospital Southampton NHS Foundation Trust**
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

**Study participating centre**
**United Leeds Teaching Hospitals NHS Trust**
Leeds Gen Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

# Sponsor information

**Organisation**
University of Dundee

**ROR**
https://ror.org/03h2bxq36

# Funder(s)

**Funder type**
Industry

**Funder Name**
Platinum Informatics Ltd

# Results and Publications

## Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |
| Other unpublished results | | | 29/01/2025 | No | No |
| Participant information sheet | version 1 | 17/05/2022 | 19/08/2022 | No | Yes |
| Participant information sheet | version 2 | 19/08/2022 | 05/09/2022 | No | Yes |
| Protocol file | version 1 | 17/05/2022 | 19/08/2022 | No | No |