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Evaluating the performance of a blood test to detect the mechanisms of resistance to trastuzumab therapy in stomach and gullet (gastroesophageal) cancer

Submission date
12/11/2020

Recruitment status
No longer recruiting

Registration date
08/04/2021

Overall study status
Completed

Last Edited
08/04/2021

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
HER2-positive cancer is a cancer that has higher than normal levels of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. Patients with HER2-positive cancer are eligible for therapy with the drug trastuzumab (also named Herceptin). Trastuzumab can help control the growth of cancer cells containing high amounts of HER2. However, trastuzumab resistance can occur and the cancer that has been responding to the therapy starts to resist the effects of the therapy and begins to grow (disease progression). When this happens, alternative therapies and management need to be discussed. To select the most appropriate treatment, the precise resistance mechanisms in each patient's cancer need to be identified. This can be achieved by analysing the DNA of tumour tissue obtained via biopsy. But this procedure is invasive and often not possible. Recently, a new test that requires a blood sample has been developed. It is called a liquid biopsy and it uses the pieces of DNA from tumour cells that are in the bloodstream. The aim of the REGAL study is to evaluate the performance of liquid biopsies in detecting the mechanisms of trastuzumab resistance in HER2 positive gastroesophageal cancers and to assess if liquid biopsies could be an alternative to tissue biopsies. This would provide a less invasive and more useful test that could be used to closely monitor patients on treatment.

Who can participate?
Patients diagnosed with a HER2 positive oesophageal or stomach cancer and being offered the therapy combining trastuzumab and chemotherapy.

What does the study involve?
Blood samples will be collected at the start of the trastuzumab and chemotherapy. If there is evidence the cancer is resisting the trastuzumab and chemotherapy (disease progression), another blood sample will be collected at this time. Optionally, if the participant is willing to,

tumour tissue samples will also be collected at the same times. We will analyse the DNA contained in the blood samples to see if information about any mechanisms of resistance can be detected and if this information is concordant with information from tissue biopsies.

What are the possible benefits and risks of participating?
There is no apparent direct benefit in taking part in the research. However, the information obtained from this study will be extremely useful to assess the clinical value of liquid biopsy. What is learnt from this study could benefit patients with the same type of cancer in the future. There is no risk associated with the blood sampling procedure. The samples will be collected at the same time as participants undergo routine blood tests, so it will not require additional needles for blood collection. For tissue biopsy samples (optional), wherever possible, they will be collected when the participants undergo biopsy procedures as part of their routine care. If not possible, then the biopsies will be carried out for the study purpose only. Collecting these tissue specimens is considered safe, but the possible risks include bleeding, infection and pain at the time the samples are removed. Such complications are reported in 1 in 1000 endoscopic biopsies and in less than 1 in 100 CT-guided biopsies.

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

When is the study starting and how long is it expected to run for?
October 2020 to October 2022

Who is funding the study?
The University of Dundee (UK)

Who is the main contact?
Professor Russell Petty
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
278314

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 278314

Study information

Scientific Title
Capturing trastuzumab REsistance in Gastroesophageal Adenocarcinoma by Liquid biopsy

Acronym
REGAL

Study objectives
Liquid biopsies analyses can be used to capture the molecular mechanisms of trastuzumab resistance in advanced HER2 positive gastroesophageal adenocarcinoma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/10/2020, East of Scotland Research Ethics Service (Tayside medical Science Centre, Residency Block Level 3, George Pirie Way, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK; +44 (0)1382 383848; tay.eosres@nhs.scot), ref 20/ES/0090

Study design
Multicentre observational study with longitudinal specimen collection

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced HER2 positive gastroesophageal adenocarcinoma

Interventions
Blood samples will be collected from participants at the start of the chemotherapy + trastuzumab therapy and will be analysed by NGS to capture the molecular mechanisms involved in trastuzumab resistance. Tissue biopsies of primary tumour and metastatic sites will be also be collected from patients who are willing (optional) and profiled by NGS. This is to confirm the clinical relevance of ctDNA analysis by comparison with standard tumour tissue analysis.

Intervention Type
Genetic

Primary outcome(s)
Detection at relapse of molecular abnormalities related to trastuzumab resistance by ctDNA profiling of biopsy taken at a single time point

Key secondary outcome(s))
Using biopsy taken at a single time point:
1. Detection of molecular abnormalities using liquid biopsy
2. Detection of molecular abnormalities using the standard of care tissue biopsy analysis
2. Identification of new or known resistance-related gene variants using next generation sequencing-based ctDNA profiling and definition of a correlation between the genotype of the primary tumour and the emergence of molecularly different clones

Completion date
01/10/2022

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Willing to provide written informed consent
3. Diagnosed with histologically confirmed locally advanced or metastatic HER2 positive gastroesophageal adenocarcinoma
4. Subject is being considered for treatment with the standard of care platinum fluoropyrimidine combination chemotherapy plus trastuzumab therapy and is willing and able to proceed with this treatment
5. Subject is able to provide whole blood at baseline visit and final visit

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any medical or mental condition that would interfere with the subject’s ability to willingly give written informed consent
2. Any significant medical condition that in the opinion of the chief investigator would impair the ability of the participant to complete the requirements of the protocol

Date of first enrolment
01/12/2020

Date of final enrolment
01/10/2022

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Ninewells Hospital and Medical School
James Arrott Dr
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DD1 9SY

Study participating centre
Belfast City Hospital
10 Jubilee Rd
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Study participating centre
Velindre Cancer Centre
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Study participating centre
Edinburgh Cancer Centre - Western General Hospital
Crewe Road
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Beatson West of Scotland Cancer Centre
1053 Great Western Road
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Study participating centre
Leeds Cancer Centre
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Leeds
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Sponsor information

Organisation
University of Dundee

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Ninewells hospital Cancer Campaign

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes