ISRCTN17468602 https://doi.org/10.1186/ISRCTN17468602

Can Selumetinib make advanced thyroid cancer sensitive to radioactive iodine therapy again?

Submission date 02/12/2015	**Recruitment status** Stopped	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data [_] Record updated in last year
Registration date 02/12/2015	**Overall study status** Stopped	
Last Edited 03/11/2021	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-selumetinib-for-thyroid-cancer-that-has-stopped-taking-up-radioactive-iodine-sel

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-002269-47

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

19937

Study information

Scientific Title
SEL-I-METRY: Investigating the potential clinical benefit of Selumetinib in resensitising advanced iodine refractory differentiated thyroid cancer to radioiodine therapy

Acronym
SEL-I-METRY

Study objectives
The aim of this study is to determine the proportion of patients for whom treatment with Selumetinib increases the amount of radioactive iodine taken up by the previously iodine-refractory thyroid cancers following a short course (4 weeks) of the drug.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands – Leicester South Research Ethics Committee, 02/12/2015, ref: 15/EM/0455

Study design
Non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
Participants will receive an initial I-123 SPECT/CT scan (under rhTSH stimulation) to determine baseline iodine uptake in thyroid cancer lesions. Participants will then receive Selumetinib in a tablet form, which they are to take home and administer according to the dosing schedule (150mg/day, therefore 6 x 25mg tablets, 3 twice per day).

Participants will then undergo another I-123 SPECT/CT after this 28-day period to determine if the iodine uptake in their thyroid cancer lesions has increased. If iodine uptake has increased sufficiently, participants will be referred for further I-131 therapy. Participants will be asked to continue taking Selumetinib from the time that they have the second I-123 scan to the time they receive their I-131. Participants who do not go on the receive I-131 therapy may stop Selumetinib treatment.

The total duration of the treatment will depend on the elapsed time between the second I-123 SPECT/ CT scan, the decision about I-131 therapy being made, and the I-131 therapy being received. The minimum duration of Selumetinib therapy is approximately 28 days. The maximum may be longer (up to 50 days).

Participants who do not go on to receive I-131 will have a single follow-up appointment 30 days after the final dose of Selumetinib. Participants who do go on to receive I-131 will be followed up three-monthly for one year, and then six-monthly until the end of the trial.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Selumetinib

Primary outcome measure
Progression-free survival is determined at 12 months.

Secondary outcome measures
1. Safety is determined based on the occurrence of SAEs, SARs and SUSARs at 48 months
2. Toxicity is determined by the total number of adverse reactions, as graded by CTCAE V4.0, as identified in routine clinical assessments at each centre at 48 months
3. Radiological response rate for patients receiving radioiodine therapy is recorded at 48 months using ongoing CT scans (every 3 months for the first 6 months and then every 6 months thereafter)
4. Overall survival is determined from medical records at 48 months
5. Sufficient iodine uptake is assessed centrally using pre-defined criteria (an increase of 30% from baseline in participants who demonstrated baseline radioiodine uptake, or an increase of any level for participants who have no baseline radioiodine uptake) on an ongoing basis, with a report being collated at 48 months

Overall study start date
01/02/2015

Completion date
05/11/2020

Reason abandoned (if study stopped)
Slow recruitment and a lower than expected number of patients achieving increased iodine uptake after Selumetinib.

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 03/11/2021:
1. Diagnosed with locally advanced or metastatic differentiated thyroid cancer (papillary, follicular, Hürthle cell, or poorly differentiated carcinoma) with at least one measurable lesion as measured by computed tomography (CT) or magnetic resonance imaging (MRI)
2. Participants must have iodine refractory disease, defined below:
2.1. One or more measurable lesions that do not demonstrate iodine uptake on a previous radioiodine scan (diagnostic uptake or post therapy)
OR
2.2. One or more measurable lesions that have progressed by RECIST 1.1 criteria within 12 months of I131 therapy, despite demonstrable radioiodine avidity at the time of that treatment
3. Participants must have radiological progression by RECIST 1.1 criteria within the prior 12 months
4. Measurable disease by RECIST 1.1 criteria. Baseline scan must be completed within 4 weeks prior to the start of treatment.
5. ECOG Performance Status = 1 and able to tolerate radioiodine therapy
6. Life expectancy of at least 12 weeks
7. Required laboratory values within 14 days of day 1 of treatment:
7.1. Adequate thyroidstimulating hormone (TSH) suppression < 0.5 mU/L
7.2. Creatinine clearance >50 ml/min,
7.3. Absolute Neutrophil Count =1.5x109/L (1500 per mm3)
7.4. Platelets =100x109/L (100,000 per mm3)
7.5. Haemoglobin >9.0 g/dL
7.6. Serum bilirubin =1.5 x upper limit of normal (ULN)
7.7. Patients with no liver metastasis must have AST or ALT = 2.5 x ULN
7.8. Patients with liver metastasis must have AST or ALT = 5 x ULN. If patients have AST or ALT > 3.5 x ULN and = 5 x ULN they must have an ALP= 6 x ULN
8. Patient's with Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the
absence of evidence of haemolysis or hepatic pathology) will be eligible.
9. Able to give informed consent and willing to follow trial protocol.
10. Aged over 18
11. Female participants of childbearing potential must have a negative pregnancy test within 24 hours prior to starting therapy and agree to use dual methods of contraception for the duration of the trial and 6 months after completing treatment. Male participants must agree to use a barrier method of contraception for the duration of the trial and 4 months after completing treatment, if sexually active with a female of childbearing
potential.

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OR
2.2. One or more measurable lesions that have progressed by RECIST 1.1 criteria within 12 months of I131 therapy, despite demonstrable radioiodine avidity at the time of that treatment

3. Participants must have radiological progression by RECIST 1.1 criteria within the prior 12 months
4. Measurable disease by RECIST 1.1 criteria.
5. ECOG Performance Status = 1 and able to tolerate radioiodine therapy
6. Life expectancy of at least 12 weeks
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potential.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 60; UK Sample Size: 60

Total final enrolment
30

Key exclusion criteria
Current participant exclusion criteria as of 03/11/2021:
1. Foci of anaplastic thyroid cancer identified on histology
2. Able to receive curative surgery or radiation therapy
3. Major surgery with the exception of surgical placement for vascular access, open biopsy, or significant traumatic injury = 30 days prior to registration

4. Previous or concurrent cancer distinct in primary site or histology from thyroid cancer within previous 5 years, except for cervical cancer in situ, treated basal cell carcinoma, squamous cell carcinoma of the skin or superficial bladder tumour
5. Have received or are receiving an IMP or other systemic anticancer treatment within 4 weeks prior to the first dose of study treatment (6 weeks for nitrosoureas, mitomycin, and suramin), or within a period during which the IMP or anticancer treatment has not been cleared from the body (e.g. a period of 5 'halflives'), whichever is the most appropriate and as judged by the investigator
6. Any unresolved toxicity =CTCAE Grade 2 from previous anticancer therapy, except for alopecia
7. Prior exposure to Tyrosine Kinase, MEK, RAS or RAF inhibitors
8. Known or suspected allergy to Selumentinib or hypersensitivity to Selumetinib or any excipient agents or history of allergic reactions attributed to compounds of similar chemical or biologic composition to Selumetinib
9. Known or suspected brain metastases or spinal cord compression, unless the condition has been asymptomatic, has been treated with surgery and / or radiation, and has been stable without requiring corticosteroids nor anticonvulsant medications for at least 4 weeks prior to the first dose of study medication
10. Requiring medication with high iodine content (e.g. amiodarone)
11. Participants who have had a iodine contrast enhanced CT scan in previous 2 months
12. Ophthalmological conditions as follows:
12.1 Intra-ocular pressure >21 mmHg, or uncontrolled glaucoma (irrespective of intra-ocular pressure)
12.2 Current or past history of retinal pigment epithelial detachment (REPD)/central serous retinopathy or retinal vein occlusion
13. Any of the following cardiac conditions:
13.1 Uncontrolled hypertension (BP >150/95 mmHg despite medical therapy)
13.2 Acute coronary syndrome within 6 months prior to starting treatment
13.3 Uncontrolled angina (Canadian Cardiovascular Society grade II-IV despite medical therapy)
13.4 Symptomatic heart failure (NYHA grade II-IV), prior or current cardiomyopathy, or severe vascular disease
13.5 Prior or current cardiomyopathy including but not limited to the following:
13.5.1 known hypertrophic cardiomyopathy
13.5.2 known arrhythmogenic right ventricular cardiomyopathy
13.6 Severe valvular heart disease
13.7 Left ventricular ejection fraction <55% measured by echocardiography
13.8 Atrial fibrillation with a ventricular rate >100 bpm on ECG at rest
13.9 QTcF >450ms or other factors that increase the risk of QT prolongation
14. Participants known to be infected with human immunodeficiency virus (HIV) or hepatitis B

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9. Known or suspected brain metastases or spinal cord compression, unless the condition has been asymptomatic, has been treated with surgery and / or radiation, and has been stable without requiring corticosteroids nor anticonvulsant medications for at least 4 weeks prior to the first dose of study medication
10. Requiring medication with high iodine content (e.g. amiodarone)
11. Participants who have had a iIodine contrast enhanced CT scan in previous 2 months

Date of first enrolment
01/09/2016

Date of final enrolment
31/08/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
The Christie
Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre
Churchill Hospital
Old Road
Oxford

United Kingdom
OX3 7LE

Study participating centre
The Royal Marsden
203 Fulham Road
Chelsea
London
United Kingdom
SW3 6JJ

Study participating centre
University Hospital Southampton
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
The Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Trust

Sponsor details
Royal Hallamshire Hospital
Glossop Road
Sheffield
England
United Kingdom
S10 2JF

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Senofi-Genzyme

Results and Publications

Publication and dissemination plan
Intended publication of a study protocol and the study results upon completion of data analysis after the end of the trial.

Intention to publish date
05/11/2021

Individual participant data (IPD) sharing plan
Any requests for trial data will be reviewed by the trial management group in the first instance. Only requests that have a methodologically sound proposal and whose proposed use of the data has been approved by the independent trial steering committee will be considered. Proposals should be directed to the corresponding author in the first instance; to gain access, data requestors will need to sign a data access agreement.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	14/06/2019	08/12/2020	Yes	No
Basic results	version 1.0	03/11/2021	03/11/2021	No	No
HRA research summary			28/06/2023	No	No