

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

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| Submission date 02/12/2015 | Recruitment status Stopped | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 02/12/2015 | Overall study status Stopped | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 03/11/2021 | Condition category Cancer | <input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year |

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

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 to 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 $= 1.5 \times 10^9/L$ (1500 per mm³)
 - 7.4. Platelets $= 100 \times 10^9/L$ (100,000 per mm³)
 - 7.5. Haemoglobin > 9.0 g/dL
 - 7.6. Serum bilirubin $= 1.5 \times$ upper limit of normal (ULN)
 - 7.7. Patients with no liver metastasis must have AST or ALT $= 2.5 \times$ ULN
 - 7.8. Patients with liver metastasis must have AST or ALT $= 5 \times$ ULN. If patients have AST or ALT $> 3.5 \times$ ULN and $= 5 \times$ ULN they must have an ALP $= 6 \times$ 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.

Previous participant inclusion criteria:

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.
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 = $1.5 \times 10^9/L$ (1500 per mm³)
 - 7.4. Platelets = $100 \times 10^9/L$ (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.
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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 Selumetinib 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

Previous participant exclusion criteria:

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

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7. Prior exposure to Tyrosine Kinase, MEK, RAS or RAF inhibitors
8. Known or suspected allergy to Selumetinib 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

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 |