

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

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 30/03/2026	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

Contact name

Mrs Jayne Swain

Contact details

University of Leeds
Clinical Trials Research Unit (CTRU)
Woodhouse Lane
Leeds
United Kingdom
LS2 9JT
0113 343 4108
j.swain@leeds.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

2015-002269-47

Protocol serial number

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

Study type(s)

Treatment

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(s)

Progression-free survival is determined at 12 months.

Key secondary outcome(s)

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

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.

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 =1.5x10⁹/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.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 years

Upper age limit

110 years

Sex

All

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

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

Date of first enrolment

01/09/2016

Date of final enrolment

31/08/2019

Locations

Countries of recruitment

United Kingdom

England

Scotland

Study participating centre

Bristol Haematology and Oncology Centre

Horfield Road

Bristol

England

BS2 8ED

Study participating centre

The Christie

Wilmslow Road

Manchester

England

M20 4BX

Study participating centre

Churchill Hospital

Old Road

Oxford

England

OX3 7LE

Study participating centre

The Royal Marsden

203 Fulham Road

Chelsea

London

England

SW3 6JJ

Study participating centre

University Hospital Southampton

Tremona Road
Southampton
England
SO16 6YD

Study participating centre**Royal Surrey County Hospital**

Egerton Road
Guildford
England
GU2 7XX

Study participating centre**The Beatson West of Scotland Cancer Centre**

1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre**Nottingham City Hospital**

-
Nottingham
England
NG5 1PB

Sponsor information

Organisation

Sheffield Teaching Hospitals NHS Trust

ROR

<https://ror.org/018hjpz25>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), 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, AZ

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

United Kingdom

Funder Name

Senofi-Genzyme

Results and Publications

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
Plain English results		30/03/2026	30/03/2026	No	Yes