Clinical trial results:
A Phase II, Open-Label Study to Assess Safety and Clinical Utility of 68Ga-THP-PSMA PET/CT in Patients with High-Risk Primary Prostate Cancer or Biochemical Recurrence after Radical Treatment

Summary

EudraCT number	2017-005010-59
Trial protocol	GB
Global end of trial date	12 June 2019

Results information

Result version number	v1 (current)
This version publication date	31 January 2020
First version publication date	31 January 2020
Summary attachment (see zip file)	THERAG0001 CSR Synopsis (THERAG0001_CSR Synopsis_EudraCT.pdf)

Trial information

Trial identification

Sponsor protocol code	THERAG0001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03617588
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Theragnostics Ltd
Sponsor organisation address	2 Arlington Square, Bracknell, United Kingdom, RG12 1WA
Public contact	Michael Ferris, Clinical Trials Coordinator, Theragnostics Ltd, +44 3306067437, michael.ferris@theragnostics.com
Scientific contact	Dr Daniel Stevens, Chief Medical Officer, Theragnostics Ltd, daniel.stevens@theragnostics.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2019
Global end of trial reached?	Yes
Global end of trial date	12 June 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was:
- To evaluate 68Ga-PSMA PET/CT impact on the management of patients with prostate cancer (PCa) in the setting of:
i) Biochemical recurrence (BCR) in patients treated with prior radical prostatectomy (RP);
ii) BCR in patients treated with prior radiotherapy;
iii) Newly diagnosed high-risk PCa.

The secondary objective of the trial was:
- To evaluate the safety of 68Ga-PSMA in patients with PCa.

Protection of trial subjects:

As per attached synopsis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 49
Worldwide total number of subjects	49
EEA total number of subjects	49

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	22

From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single-centre study conducted at one site in the United Kingdom.

Pre-assignment

Screening details:

This was an open-label study to assess the safety and clinical utility of 68Ga-THP-PSMA PET/CT in patients with high-risk primary PCa or BCR after radical treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study. No blinding was necessary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Patients with newly diagnosed primary high-risk PCa who were scheduled for RP surgery.

Arm type	Experimental
Investigational medicinal product name	68Ga-THP-PSMA
Investigational medicinal product code	
Other name	Galliprost
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

68Ga-THP-PSMA was provided as a sterile solution for injection. Prior to PET/CT, 160±30 megabecquerels (MBq) 68Ga-THP PSMA was administered in a single intravenous bolus. The administration was by a slow push over a period of 1 minute, followed by a 10 mL saline flush. 68Ga-THP PSMA was injected via a cannula with the patient lying in a supine position and in an antecubital vein (or another vein that could provide access).

Arm title	Groups B and C

Arm description:

Group B - patients with PCa and a diagnosis of BCR, previously treated with RP and being considered for radical salvage therapy (with curative intent).
Group C - patients with PCa and a diagnosis of BCR, previously treated with radical radiotherapy and being considered for radical salvage therapy (with curative intent).

Arm type	Experimental
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Number of subjects in period 1	Group A	Groups B and C
Started	20	29
Completed	19	29
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Patients with newly diagnosed primary high-risk PCa who were scheduled for RP surgery.	
Reporting group title	Groups B and C
Reporting group description:	
Group B - patients with PCa and a diagnosis of BCR, previously treated with RP and being considered for radical salvage therapy (with curative intent). Group C - patients with PCa and a diagnosis of BCR, previously treated with radical radiotherapy and being considered for radical salvage therapy (with curative intent).	

Reporting group values	Group A	Groups B and C	Total
Number of subjects	20	29	49
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	14	22
From 65-84 years	12	15	27
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	20	29	49

Subject analysis sets	
Subject analysis set title	Safety Evaluable Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received a 68Ga-THP-PSMA PET/CT dose, regardless of whether they received the full intended dose, or proceeded to undergo the intended 68Ga-THP-PSMA PET/CT scan.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
A subset of the safety population who underwent the Visit 2 68Ga-THP-PSMA PET/CT scan, regardless of whether the scan was a technical success or failure.	
Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol
Subject analysis set description:	
A subset of the Full Analysis Set with at least one technically successful post baseline 68Ga-THP-PSMA PET/CT scan and without any major protocol deviations.	

Reporting group values	Safety Evaluable Population	Full Analysis Set	Per Protocol Population
Number of subjects	49	49	49
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	22	22
From 65-84 years	27	27	27
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	49	49	49

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

Patients with newly diagnosed primary high-risk PCa who were scheduled for RP surgery.

Reporting group title	Groups B and C

Reporting group description:

Group B - patients with PCa and a diagnosis of BCR, previously treated with RP and being considered for radical salvage therapy (with curative intent).
Group C - patients with PCa and a diagnosis of BCR, previously treated with radical radiotherapy and being considered for radical salvage therapy (with curative intent).

Subject analysis set title	Safety Evaluable Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received a 68Ga-THP-PSMA PET/CT dose, regardless of whether they received the full intended dose, or proceeded to undergo the intended 68Ga-THP-PSMA PET/CT scan.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

A subset of the safety population who underwent the Visit 2 68Ga-THP-PSMA PET/CT scan, regardless of whether the scan was a technical success or failure.

Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

A subset of the Full Analysis Set with at least one technically successful post baseline 68Ga-THP-PSMA PET/CT scan and without any major protocol deviations.

Primary: Change in management plan

End point title	Change in management plan[1]

End point description:

The impact of 68Ga-THP-PSMA PET/CT on the management of patients with PCa was analysed by measuring the percentage of patients who had a change in management plan as a result of 68Ga-THP-PSMA PET/CT documented after scan, compared with their pre-scan management plan. A change status of 'Yes' was assigned if there was any difference in treatment options between the intended and revised management plans. A change status of 'No' was assigned if the intended and revised management plans remained identical. This endpoint was assessed in the full analysis set, but as a sensitivity analysis, was also assessed in the per protocol population in case there was a difference between the populations. As all 49 patients underwent a technically successful post-baseline scan, the full analysis set and per protocol populations were the same.

End point type	Primary

End point timeframe:

Details of intended pre-scan patient management plans were collected at Visit 1 (within four weeks of the scan) and compared with post 68Ga-THP-PSMA PET/CT scan management plans collected at Visit 4 (approximately 2 weeks post-scan).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint, the percentage of patients who had a change in management plan as a result of 68Ga-THP PSMA PET/CT documented after scan compared with pre-scan management plan, was analysed descriptively.

End point values	Group A	Groups B and C	Full Analysis Set	Per Protocol Population
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	20	29	49	49
Units: Number of patients				
Change in management plan	6	15	21	21
No change in management plan	14	14	28	28

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety

End point description:

Safety was assessed by means of physical examination, vital signs, cardiovascular profile, performance status, laboratory evaluations (haematology, biochemistry, urinalysis and prostate-specific antigen), recording of concurrent illness/therapy and AEs. No dose limiting toxicity was defined in this study.

End point type	Secondary

End point timeframe:

Safety was assessed at screening, during the study and at Visit 4. AEs, regardless of relationship to study treatment, were recorded from the time of 68Ga-THP-PSMA administration until 30 days after the administration of 68Ga-THP-PSMA.

End point values	Group A	Groups B and C	Safety Evaluable Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	29	49	
Units: Number of patients with events				
Any TEAE	2	3	5	
Any TEAE related to 68Ga-THP-PSMA	1	1	2	
Any TEAE CTCAE Grade 3 or higher	1	1	2	
Any related TEAE CTCAE Grade 3 or higher	0	0	0	
Any TEAE with outcome of death	0	0	0	
Any related TEAE with outcome of death	0	0	0	
Any serious TEAE	0	0	0	
Any serious TEAE related to 68Ga-THP-PSMA	0	0	0	
Any TEAE leading to discontinuation from study	0	0	0	
Any related TEAE leading to discontinuation	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety was assessed at screening, during the study and at Visit 4. AEs, regardless of relationship to study treatment, were recorded from the time of 68Ga-THP-PSMA administration until 30 days after the administration of 68Ga-THP-PSMA.

Adverse event reporting additional description:

Safety was assessed by means of physical examination, vital signs, cardiovascular profile, performance status, laboratory evaluations (haematology, biochemistry, urinalysis and prostate-specific antigen), recording of concurrent illness/therapy and AEs. No dose limiting toxicity was defined in this study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Group A

Reporting group description:

Patients with newly diagnosed primary high-risk PCa who were scheduled for RP surgery.

Reporting group title	Groups B and C

Reporting group description:

Group B - patients with PCa and a diagnosis of BCR, previously treated with RP and being considered for radical salvage therapy (with curative intent).
Group C - patients with PCa and a diagnosis of BCR, previously treated with radical radiotherapy and being considered for radical salvage therapy (with curative intent).

Reporting group title	Safety Evaluable Population

Reporting group description:

All patients who received a 68Ga-THP-PSMA PET/CT dose, regardless of whether they received the full intended dose, or proceeded to undergo the intended 68Ga THP PSMA PET/CT scan.

Serious adverse events	Group A	Groups B and C	Safety Evaluable Population
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 29 (0.00%)	0 / 49 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Group A	Groups B and C	Safety Evaluable Population
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	3 / 29 (10.34%)	5 / 49 (10.20%)
Injury, poisoning and procedural complications			

Thermal burn			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 20 (5.00%)	0 / 29 (0.00%)	1 / 49 (2.04%)
occurrences (all)	2	0	2
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Sensory loss			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Catheter site rash			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 29 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 29 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 20 (5.00%)	0 / 29 (0.00%)	1 / 49 (2.04%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 29 (3.45%)	1 / 49 (2.04%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 October 2018	This amendment resulted in protocol version 2.0, dated 29 October 2018. The following changes were made: Inclusion and exclusion criteria were updated to provide greater detail and clarity for each criterion. Schedule of events was updated to remove Visit 5. A single interim analysis was introduced to provide some early indication of the study results and to consider the primary study outcome, patient background and management. Additional administrative corrections (spelling mistakes and formatting) were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 May 2019	The decision was made to terminate the study early on 20 May 2019 as there was considered to be sufficient safety and efficacy data available to perform the outcome analysis. There were no consequences to the overall risk benefit assessment of the IMP as the decision to stop the trial was not based on safety grounds or toxicity. Three patients were still on study at the time of early termination and continued on study until their last visit.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As per the protocol, 20 patients were planned to be enrolled into Group C. However, only 8 patients were enrolled. This was due to a very high change in management rates and difficulty recruiting at site due to their clinical practice preferences.

Notes: