Clinical trial results:
A phase II single arm, multi-centre trial of triamcinolone with a GnRH analog for castration resistant prostate cancer

Summary

EudraCT number	2010-022010-32
Trial protocol	GB
Global end of trial date	24 September 2020

Results information

Result version number	v1 (current)
This version publication date	09 March 2024
First version publication date	09 March 2024
Summary attachment (see zip file)	Summary of Outputs (TRICREST - Final analysis outputs _25.11.2022.pdf)

Trial information

Trial identification

Sponsor protocol code	PR201005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	Joint Research and Management Office, 5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Jonathan Shamash, Barts Health NHS Trust, +44 2034657108, jonathan.shamash2@nhs.net
Scientific contact	Jonathan Shamash, Barts Health NHS Trust, +44 2034657108, jonathan.shamash2@nhs.net

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	22 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 September 2020
Global end of trial reached?	Yes
Global end of trial date	24 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To examine whether triamcinolone (IM injection) offers an increased progression free survival (PFS) in patients with confirmed castration resistant prostate cancer (CRPC).

Protection of trial subjects:

Following failure of ADT treatment, giving standard care dexamethasone, CRPC patients, have a resulting 50% response rate and an average of 4 months until progression. There remains a need to increase duration of response in this group of patients. The treatment of CRPC with triamcinolone is based on the understanding that CRPC is, in part, caused by mutational androgen receptor binding; using triamcinolone to suppress endogenous corticosteroids, results in a failure to stimulate those mutants with a promiscuous receptor which are able to proliferate through activation by adrenal steroids.

A formal interim analysis of the accumulated data was performed after the 35th patient in order to assess the effect of the trial IMP on the primary endpoint.

The purposes for the interim analysis were to:
o Assess the safety of the study treatment;
o Stop the trial early due to futility

If the results of the interim analysis indicated that there were 14 or less progression free survivors out of 35, the trial would be stopped.

Risk management
In the published study, treatment was well tolerated with no grade 3 or 4 toxicities were observed and the increased risk to hyperglycaemic patients was controlled by close monitoring of serum glucose and subsequent increases in anti diabetic medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 55
Worldwide total number of subjects	55
EEA total number of subjects	0

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)	8
From 65 to 84 years	44
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

A total of 63 evaluable patients with an interim analysis after recruitment of 35 patients were planned to be recruited to the study. However, end of recruitment was deemed to be when 29 patients survived progression free for 6 months. In total 55 evaluable patients were recruited between Jan 2012 and September 2020.

Pre-assignment

Screening details:

55 evaluable patients were recruited to the study between 01 March 2012 and 03 October 2016. There were no screen failures.

Period 1

Period 1 title	Recruitment (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Tiamcinolone and GnRH

Arm description:

intra-muscular (IM) triamcinolone with a GnRH analog for castration resistant prostate cancer (CRPC). Patients will have a loading dose of 360mg on Cycle 1 Day 1.
On cycle 2 Day 1, patients will receive a lower dose of 120mg of Triamcinolone. From cycle 3 onwards, patients' dose will depend on their cortisol results. If patients' blood cortisol is >30nmol/l, then their dose will be increased to 200mg otherwise their dose will remain at 120mg for that cycle and their cortisol tested again before the next cycle.

Arm type	Experimental
Investigational medicinal product name	Triamcinolone
Investigational medicinal product code	
Other name	Kenalog
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Injection

Dosage and administration details:

Patients were given a loading dose of 360mg on Cycle 1 Day 1 given by IM injection. On cycle 2 Day 1, patients received a lower dose of 120mg of Triamcinolone by injection. From cycle 3 onwards, patients' dose was dependent on their cortisol results. If patients' blood cortisol is >30nmol/l, then their dose was increased to 200mg otherwise their dose remained at 120mg for that cycle and their cortisol tested again before the next cycle.

Number of subjects in period 1	Tiamcinolone and GnRH
Started	55
Completed	55

Baseline characteristics

Reporting groups	
Reporting group title	Recruitment

Reporting group description: -

Reporting group values	Recruitment	Total	
Number of subjects	55	55	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	44	44	
85 years and over	3	3	
Gender categorical Units: Subjects			
Female	0	0	
Male	55	55	

End points

End points reporting groups

Reporting group title	Tiamcinolone and GnRH
Reporting group description:	
intra-muscular (IM) triamcinolone with a GnRH analog for castration resistant prostate cancer (CRPC). Patients will have a loading dose of 360mg on Cycle 1 Day 1. On cycle 2 Day 1, patients will receive a lower dose of 120mg of Triamcinolone. From cycle 3 onwards, patients' dose will depend on their cortisol results. If patients' blood cortisol is >30nmol/l, then their dose will be increased to 200mg otherwise their dose will remain at 120mg for that cycle and their cortisol tested again before the next cycle.	
Subject analysis set title	Evaluable Population
Subject analysis set type	Per protocol
Subject analysis set description:	
Evaluable population is defined as all patients enrolled into the trial who completed at least 2 cycles of study medication and 12 weeks of follow-up.	

Primary: Progression Free Survival at 6 months

End point title	Progression Free Survival at 6 months
End point description:	
End point type	Primary
End point timeframe:	
6 months	

End point values	Tiamcinolone and GnRH	Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	55	40		
Units: month				
median (confidence interval 95%)	8.6 (6.4 to 17.6)	9 (7.6 to 19.6)		

Statistical analyses

Statistical analysis title	Progression Free Survival
Comparison groups	Tiamcinolone and GnRH v Evaluable Population
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Cox proportional hazard
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.4
upper limit	20.3

Secondary: Time to PSA Progression

End point title	Time to PSA Progression

End point description:

End point type	Secondary

End point timeframe:

Time to prostate specific antigen progression from baseline

End point values	Tiamcinolone and GnRH	Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	55	40		
Units: month				
median (confidence interval 95%)	6.5 (4.0 to 14.6)	10.9 (4.6 to 15.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Circulating Tumour Cells Response

End point title	Circulating Tumour Cells Response

End point description:

Baseline values presented only

End point type	Secondary

End point timeframe:

Baseline to Cycle 1 Day 28

End point values	Tiamcinolone and GnRH	Evaluable Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	24		
Units: cells				
arithmetic mean (standard deviation)	23.9 (± 68.9)	7.3 (± 11.5)		

Statistical analyses

Statistical analysis title	Change between baseline and C1D28
Comparison groups	Tiamcinolone and GnRH v Evaluable Population
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.714
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to end of treatment

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Tiamcinolone and GnRH

Reporting group description:

intra-muscular (IM) triamcinolone with a GnRH analog for castration resistant prostate cancer (CRPC). Patients will have a loading dose of 360mg on Cycle 1 Day 1.
On cycle 2 Day 1, patients will receive a lower dose of 120mg of Triamcinolone. From cycle 3 onwards, patients' dose will depend on their cortisol results. If patients' blood cortisol is >30nmol/l, then their dose will be increased to 200mg otherwise their dose will remain at 120mg for that cycle and their cortisol tested again before the next cycle.

Serious adverse events	Tiamcinolone and GnRH		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 55 (49.09%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Hypertension			
subjects affected / exposed	18 / 55 (32.73%)		
occurrences causally related to treatment / all	18 / 23		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin atrophy			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Tiamcinolone and GnRH		
Total subjects affected by non-serious adverse events subjects affected / exposed	55 / 55 (100.00%)		
Cardiac disorders Hypertension subjects affected / exposed occurrences (all)	24 / 55 (43.64%) 44		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Appetite disorder subjects affected / exposed occurrences (all)	14 / 55 (25.45%) 49 10 / 55 (18.18%) 31 4 / 55 (7.27%) 22		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 13		
Skin and subcutaneous tissue disorders Skin atrophy subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 26		
Musculoskeletal and connective tissue disorders Muscular weakness subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	9 / 55 (16.36%) 39 4 / 55 (7.27%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2012	Volume of blood for CTC samples changed from 7.5ml to 15ml
19 April 2012	New patient information sheet explaining the patient's exposure to radiation created. A separate PIS for sites where they do not consider bone scans as standard of care therefore requiring an ARSAC license and the other for sites where an ARSAC license is not necessary.
30 April 2012	Change of sponsor name from the Barts and the London NHS Trust to Barts Health NHS Trust.
04 September 2013	Updates to Interim analysis timelines, Target Accrual and TMG instead of TSC
11 February 2014	Increase of IMP dose from 120mg to 200mg if cortisol level ≥30nmol/l.
01 December 2015	Clarification that progression needs to be confirmed radiologically before a patient can be withdrawn. Information regarding PSA progression added.
27 November 2017	Updated end of trial definition

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None to report.

Notes: