Clinical trial results:
NEPTUNE: A Randomised Phase II Study of Neoadjuvant TAK-700 and Leuprorelin Acetate versus Surgery Alone in Intermediate and High Risk Clinically Localized Prostate Cancer

Summary

EudraCT number	2012-000478-42
Trial protocol	GB
Global end of trial date	16 June 2015

Results information

Result version number	v1 (current)
This version publication date	04 September 2016
First version publication date	04 September 2016

Trial information

Trial identification

Sponsor protocol code	008285QM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Queen Mary University of London
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Marjia Monsur, Centre for Experimental Cancer Medicine, Queen Mary University of London, London, EC1M 6BQ, +44 02078827351, bci-neptune@qmul.ac.uk
Scientific contact	Professor Tom Powles, Centre for Experimental Cancer Medicine, Queen Mary University of London, London, EC1M 6BQ, +44 02078828493, bci-neptune@qmul.ac.uk

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	01 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 June 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate if neoadjuvant TAK-700 with LHRH agonists and prostatectomy is associated with an improvement in progression-free survival compared to prostatectomy alone. The primary endpoint will assess the 3 year biochemical progression free survival (PSA)

Protection of trial subjects:

Both drugs are associated with side effects. These are on the whole due to testosterone reductions in the body. The side effects such as hot flushes and fatigue are common. Erectile dysfunction, which commonly occurs with the prostate surgery could be made worse. Specific side effects associated with orteronel such as swelling can also occur. This was closely monitored during and after the study. Patients on the study arm were required to attend clinic every 4 weeks whilst they were on study medication where adverse events were recorded. The patient information sheet included details on expected adverse events for patients to look out for and also details that unexpected events may occur.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	7

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 5/6/13 and 12/6/14, 16 patients in the United Kingdom with Intermediate and High Risk Clinically Localised Prostate Cancer were recruited to the NEPTUNE study.

Pre-assignment

Screening details:

Inclusion criteria included patients with intermediate and high risk clinically localised prostate cancer who had received no previous treatment. 16 patients were randomised (1:1) prior to the early termination of this study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Neoadjuvant TAK-700,leuprorelin acetate and prostatectomy

Arm description:

Neoadjuvant TAK-700, leuprorelin acetate and prostatectomy

Arm type	Experimental
Investigational medicinal product name	TAK-700 (Orteronel)
Investigational medicinal product code	
Other name	TAK-700, Orteronel
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300mg BID (Daily total dose 600mg) for 24 week period until prostatectomy

Investigational medicinal product name	Leuprorelin Acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

3.75mg every 28 days until prostatectomy

Arm title	Prostatectomy alone

Arm description:

Prostatectomy alone

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Neoadjuvant TAK-700,leuprorelin acetate and prostatectomy	Prostatectomy alone
Started	6	10
Completed	6	10

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Adults (18-64 years)	7	7	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous Units: years			
median	64.2		
inter-quartile range (Q1-Q3)	61.5 to 68.7	-	
Gender categorical Units: Subjects			
Male	16	16	
Gleason Score Units: Subjects			
3+4	8	8	
4+3	3	3	
4+4	3	3	
4+5	2	2	
T-stage Units: Subjects			
T2a	4	4	
T2c	2	2	
T3a	8	8	
T3b	2	2	
Prostate cancer risk Units: Subjects			
Intermediate	4	4	
High	12	12	
Planned Surgery Type Units: Subjects			
Robotic	14	14	
Other	2	2	
Performance Status Units: Subjects			
ECOG 1	3	3	
ECOG 0	13	13	
PSA Units: ng/mL			
median	9.6		
inter-quartile range (Q1-Q3)	7.4 to 23.5	-	

End points

End points reporting groups

Reporting group title	Neoadjuvant TAK-700,leuprorelin acetate and prostatectomy
Reporting group description:	
Neoadjuvant TAK-700, leuprorelin acetate and prostatectomy	
Reporting group title	Prostatectomy alone
Reporting group description:	
Prostatectomy alone	

Primary: Biochemical Progression Free Survival

End point title	Biochemical Progression Free Survival[1]
End point description:	
Assess the 3 year biochemical progression free survival (PSA) defined as a post-operative serum PSA of greater or equal to 0.2 ng/dl on 2 separate occasions as defined by the AUA.	
End point type	Primary
End point timeframe:	
From registration until progression	

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: Due to early termination of the study due to IMP withdrawal from development by the manufacturer, there is insufficient data to perform analysis of this endpoint.

End point values	Neoadjuvant TAK-700,leuprorelin acetate and prostatectomy	Prostatectomy alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	10		
Units: weeks	6	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From date of consent to 30 days post surgery	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 16 (25.00%)		
Cardiac disorders			
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Palmer Plantar Erythema			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2013	-Addition of a participating site -Updated IMPD -Changes to the screening procedures- MRI can occur within 16 weeks of randomisation instead of 4 weeks. -Changes to the time frame in which sites provide screening biopsy to within 8 weeks of randomisation
26 June 2014	-Change of Principal Investigator
22 September 2014	-Implementation of a temporary halt - A manufacturing stop in place concerning the investigational medicinal product ortenerol (TAK-700) by Millenium (Takeda) -Amended Investigators Brochure (updated safety information) -Updated Leuprorelin label

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 September 2014	Halt to recruitment implemented in Substantial Amendment 3. A manufacturing stop was put in place concerning the investigational medicinal product ortenerol (TAK-700) by Millenium (Takeda). Recruiting sites were asked to discontinue providing information sheets for the Neptune study to prospective trial patients. Takeda agreed to provide study medication to all patients who were still on treatment and for those patients who had been given a patient information sheet prior to the temporary halt coming into effect. Patients on treatment completed their treatment schedule as per protocol. The end of study notification was submitted to the Competent Authority once the last patient on treatment had completed the follow up period.	-

Notes:

Limitations and caveats

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

Small numbers precluded any meaningful analysis of any protocol-specified endpoints.

Notes: