Clinical trial results:
A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PROOF OF CONCEPT STUDY OF MAINTENANCE THERAPY WITH TASQUINIMOD IN PATIENTS WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER WHO ARE NOT PROGRESSING AFTER A FIRST LINE DOCETAXEL BASED CHEMOTHERAPY

Summary

EudraCT number	2012-001038-32
Trial protocol	ES BE CZ LT HU IT DK GB DE PL
Global end of trial date	20 May 2015

Results information

Result version number	v1 (current)
This version publication date	13 May 2016
First version publication date	13 May 2016
Summary attachment (see zip file)	AE details (8-55-58102-002_AE details.docx)

Trial information

Trial identification

Sponsor protocol code	8-55-58102-002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65 quai Georges Gorse, Boulogne-Billancourt, France, 92100
Public contact	Medical director, Department of Cancer Medicine, Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical director, Department of Cancer Medicine, Ipsen Pharma, clinical.trials@ipsen.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	07 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2015
Global end of trial reached?	Yes
Global end of trial date	20 May 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the clinical efficacy (i.e. radiological progression free survival [PFS]) of tasquinimod maintenance therapy with placebo in patients with metastatic castrate-resistant prostate cancer (mCRPC) who have not progressed after a first line docetaxel based chemotherapy.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21 and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2012
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	Poland: 7
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Denmark: 19
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Lithuania: 17
Worldwide total number of subjects	144
EEA total number of subjects	144

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)	28
From 65 to 84 years	115
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was performed as a multicentre study at 51 investigational sites (of which 44 randomised patients) in Belgium, Czech Republic, Denmark, France, Germany, Hungary, Italy, Lithuania, Poland, Spain and United Kingdom (UK).

Pre-assignment

Screening details:

A total of 219 patients were screened and 144 patients were randomised.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

All of the study treatments were similar in size, colour, smell, taste and appearance allowing the blinded conditions of the study to be maintained.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tasquinimod

Arm description:

1 capsule daily, taken orally with water and food (0.25 mg initially then dose escalated to 0.5 mg and then to 1 mg per day) until disease progression.

Tasquinimod: Patients received initially an oral dose of 0.25 mg/day of tasquinimod, starting on Day 1, for at least 2 weeks. Once tolerability of the 0.25 mg/day dose was established, patients received a dose increase to 0.5 mg/day for at least 2 weeks, and then increased to 1 mg/day of study treatment. Patients showing poor tolerability for the escalated doses of tasquinimod were allowed to continue study treatment at the highest individually tolerated dose

Withdrawn during treatment period 59 (AE 13, Consent withdrawn 13, Disease progression 31, Other 2)

Arm type	Active comparator
Investigational medicinal product name	tasquinimod
Investigational medicinal product code	ABR-215050
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

0.25 to 1 mg

Arm title	Placebo

Arm description:

1 capsule daily, taken orally with water and food until disease progression

Placebo: Patients received Placebo capsules (identical to tasquinimod capsules) to be taken orally once a day with water and food.

Withdrawn during treatment period 61 (AE 3, Consent withdrawn 6, Disease progression 46, Other 6)

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

0 mg

Number of subjects in period 1	Tasquinimod	Placebo
Started	71	73
Ongoing in Treatment Period:Data Cut-off	12	12
Withdrawn During Treatment:Data Cut-off	59	61
Ongoing Treatment Period:Final Analysis	0	0
Withdrawn During Treatment:Final Analysi	71	73
Completed	0	0
Not completed	71	73
Consent withdrawn by subject	13	6
Disease progression	37	50
Adverse event, non-fatal	13	3
Not Specified	8	14

Baseline characteristics

Reporting groups

Reporting group title	Tasquinimod

Reporting group description:

1 capsule daily, taken orally with water and food (0.25 mg initially then dose escalated to 0.5 mg and then to 1 mg per day) until disease progression.

Tasquinimod: Patients received initially an oral dose of 0.25 mg/day of tasquinimod, starting on Day 1, for at least 2 weeks. Once tolerability of the 0.25 mg/day dose was established, patients received a dose increase to 0.5 mg/day for at least 2 weeks, and then increased to 1 mg/day of study treatment. Patients showing poor tolerability for the escalated doses of tasquinimod were allowed to continue study treatment at the highest individually tolerated dose

Withdrawn during treatment period 59 (AE 13, Consent withdrawn 13, Disease progression 31, Other 2)

Reporting group title	Placebo

Reporting group description:

1 capsule daily, taken orally with water and food until disease progression

Placebo: Patients received Placebo capsules (identical to tasquinimod capsules) to be taken orally once a day with water and food.

Withdrawn during treatment period 61 (AE 3, Consent withdrawn 6, Disease progression 46, Other 6)

Reporting group values	Tasquinimod	Placebo	Total
Number of subjects	71	73	144
Age categorical Units: Subjects			
18 to ≤ 65 years	18	17	35
66 to ≤ 75 years	40	45	85
> 75 years	13	11	24
Age continuous			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population			
Units: years			
arithmetic mean	69.6	69.6	
standard deviation	± 7.18	± 5.57	-
Gender categorical			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population			
Units: Subjects			
Female	0	0	0
Male	71	73	144
Race			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population.			
Units: Subjects			
Black/African American	0	1	1
Caucasian/White	52	58	110
Multiple Race	1	0	1
Missing	18	14	32

Region of Enrollment			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population			
Units: Subjects			
Czech Republic	5	1	6
Belgium	5	6	11
Hungary	2	2	4
Denmark	6	13	19
Poland	4	3	7
Italy	9	5	14
United Kingdom	8	6	14
France	17	14	31
Lithuania	7	10	17
Germany	3	3	6
Spain	5	10	15
Ethnicity			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population			
Units: Subjects			
Hispanic or Latino	2	4	6
Not Hispanic or Latino	52	55	107
Missing	17	14	31
ECOG Performance Status Score			
ITT population Eastern Co-operative Oncology Group (ECOG) Score: 0=Fully active, able to carry on all pre-disease performance without restriction, 1=Restricted in physically strenuous activity, but ambulatory & able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2=Ambulatory & capable of all self-care but unable to carry out any work activities. Up & about more than 50% of waking hours, 3=Capable of limited self-care,confined to bed or chair more than 50% of waking hours, 4=Completely disabled. Totally confined to bed or chair, 5=Dead			
Units: Subjects			
0 (Normal Activity)	39	31	70
1 (Restricted Activity)	32	38	70
Missing	0	4	4
Region			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population.			
Units: Subjects			
Eastern Europe	18	16	34
Western Europe	53	57	110
Weight			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population.			
Units: kg			
arithmetic mean	83.7	83.4	
standard deviation	± 12.57	± 15.09	-
BMI			
ITT population: All randomised patients. Patients were allocated to the treatment they were randomised to. Patients randomised that have been actually dead before randomisation were not retained in the intention to treat (ITT) population.			
Units: kg/m2			

arithmetic mean	27.67	28.01	
standard deviation	± 3.543	± 4.399	-

End points

End points reporting groups

Reporting group title	Tasquinimod

Reporting group description:

1 capsule daily, taken orally with water and food (0.25 mg initially then dose escalated to 0.5 mg and then to 1 mg per day) until disease progression.

Tasquinimod: Patients received initially an oral dose of 0.25 mg/day of tasquinimod, starting on Day 1, for at least 2 weeks. Once tolerability of the 0.25 mg/day dose was established, patients received a dose increase to 0.5 mg/day for at least 2 weeks, and then increased to 1 mg/day of study treatment. Patients showing poor tolerability for the escalated doses of tasquinimod were allowed to continue study treatment at the highest individually tolerated dose

Withdrawn during treatment period 59 (AE 13, Consent withdrawn 13, Disease progression 31, Other 2)

Reporting group title	Placebo

Reporting group description:

1 capsule daily, taken orally with water and food until disease progression

Placebo: Patients received Placebo capsules (identical to tasquinimod capsules) to be taken orally once a day with water and food.

Withdrawn during treatment period 61 (AE 3, Consent withdrawn 6, Disease progression 46, Other 6)

Primary: Time to Radiological Progression Free Survival [PFS]

End point title	Time to Radiological Progression Free Survival [PFS]

End point description:

The time from the date of randomisation to the date of radiological progression or death due to any cause.

Intention to treat (ITT) Population

End point type	Primary

End point timeframe:

Every 8 weeks until disease progression documentation (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Weeks				
median (confidence interval 90%)	31.7 (24.3 to 53.7)	22.7 (16.1 to 25.9)		

Statistical analyses

Statistical analysis title	Stratified[a]

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0315 [1]
Method	Logrank

Notes:

[1] - Adjusted for visceral metastases, opioid analgesic use and region, demonstrating a reduction in the risk of progression of 40% for tasquinimod compared with placebo Method

Statistical analysis title	Unstratified[b]

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0344
Method	Logrank

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time from randomisation to death due to any cause.

ITT Population

Tasquinimod: The data for this outcome is not evaluable (NE), listed as 0. Median (90% Confidence Interval)= (NE to NE). Patients censored = 63, Patients at risk (t=0) = 71. Overall survival data are immature: only 8 deaths are reported

Placebo: The data for this outcome is not evaluable (NE), listed as 0. Median (90% Confidence Interval)= (NE to NE). Patients censored = 67, Patients at risk (t=0) = 73. Overall survival data are immature: only 6 deaths are reported

End point type	Secondary

End point timeframe:

Every 3 months after study treatment stop until death (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: weeks				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Stratified[a]

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.443 [2]
Method	Logrank

Notes:

[2] - Adjusting for presence (or absence) of visceral metastases, opioid analgesic use and region (Eastern Europe, Western Europe). One-sided p-value

Secondary: Time to Progression Free Survival [PFS] on Next-line Therapy (PFS 2)

End point title	Time to Progression Free Survival [PFS] on Next-line Therapy (PFS 2)

End point description:

The time from the date of randomisation to the date of radiological progression free survival [PFS] on next-line therapy (PFS 2) or death due to any cause.

ITT Population

Tasquinimod: Median (90% Confidence Interval)= (7.1 to 30.7). Patients censored = 28, Patients at risk (t=0) = 39.
Placebo: Median (90% Confidence Interval)= (12.6 to NA). Patients censored = 44, Patients at risk (t=0) = 47

End point type	Secondary

End point timeframe:

Every 3 months after study treatment stop (follow-up) until progression under the next line therapy (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: weeks				
number (not applicable)	19.3	24.1		

Statistical analyses

Statistical analysis title	PFS 2

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5219 [3]
Method	Logrank

Notes:

[3] - Adjusting for presence (or absence) of visceral metastases, opioid analgesic use and region (Eastern Europe, Western Europe). One-sided p-value

Secondary: Symptomatic PFS

End point title	Symptomatic PFS

End point description:

Symptomatic PFS is defined as the time from the date of randomisation to the date of symptomatic progression or death due to prostate cancer, whichever occurs first [symptomatic progression as assessed by Brief Pain Inventory (BPI) and analgesic use]

ITT Population

Tasquinimod: The data for this outcome is not evaluable (NE), listed as 0. Median (90% Confidence Interval)= (31.9 to NE). Patients censored = 48, Patients at risk (t=0) = 71

Placebo: The data for Median (90% Confidence Interval), is NE (Not evaluable). Patients censored = 54, Patients at risk (t=0) = 73

End point type	Secondary

End point timeframe:

Every 8 weeks until symptomatic or radiological progression documentation (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: weeks				
number (not applicable)	0	95.3		

Statistical analyses

Statistical analysis title	Symptomatic PFS

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5442 [4]
Method	Logrank

Notes:

[4] - Adjusting for presence (or absence) of visceral metastases, opioid analgesic use and region (Eastern Europe, Western Europe). One-sided p-value

Secondary: Time to Further Anticancer Treatment for Prostate Cancer

End point title	Time to Further Anticancer Treatment for Prostate Cancer

End point description:

Time from randomisation to further treatment for prostate cancer

ITT population

End point type	Secondary

End point timeframe:

Every 3 months after study treatment stop until further anticancer therapy for prostate cancer (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: weeks				
median (confidence interval 90%)	42.3 (32 to 58)	29 (23.1 to 39.1)		

Statistical analyses

Statistical analysis title	Time to Further Anticancer Treatment for Prostate

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112 [5]
Method	Logrank

Notes:

[5] - Adjusting for presence (or absence) of visceral metastases, opioid analgesic use and region (Eastern Europe, Western Europe). One-sided p-value

Secondary: Time to Deterioration in Functional Assessment of Cancer Therapy – Prostate (FACT-P)

End point title	Time to Deterioration in Functional Assessment of Cancer Therapy – Prostate (FACT-P)

End point description:

End of Study visit (within 14 days of last dose of study treatment)

Impact of tasquinimod on health related quality of life (QoL) - Analysis of time to deterioration in FACT-P

The FACT-P measurement system is a validated collection of health related quality of life (HRQOL) questionnaires used to assess HRQOL in men with prostate cancer. It is appropriate for use with patients with any form of cancer and extensions of it have been used and validated in other chronic illness condition. The FACT-P is a self-administered 39-item scale comprising five domains: physical well-being, social/family well-being, functional well-being, emotional well-being and additional concerns. The individual subscale scores range from 0 to a high between 24 and 48 and the total score ranges between 0 and 156, with higher scores representing better Quality of Life (QoL)

ITT Population

End point type	Secondary

End point timeframe:

Up to End of Study visit (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: weeks				
median (confidence interval 90%)	8.1 (8.1 to 13.1)	15.7 (10.6 to 16.3)		

Statistical analyses

Statistical analysis title	Stratified[a]

Statistical analysis description:

ITT Population

Comparison groups	Tasquinimod v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2491 [6]
Method	Logrank

Notes:

[6] - Comments Adjusting for presence (or absence) of visceral metastases, opioid analgesic use (or not) & region (Eastern Europe, Western Europe). One-sided p-value

Secondary: Change From Baseline of EuroQol-5 Dimension QoL Instrument (EQ-5D) VAS Score

End point title	Change From Baseline of EuroQol-5 Dimension QoL Instrument (EQ-5D) VAS Score

End point description:

Baseline is defined as the last measurement collected prior to the first dose of study drug.

End of Study visit (within 14 days of last dose of study treatment)

The EQ-5D, a 5-item scale useful in health resource utilisation and cost comparisons between the treatment groups designed for self-completion by patients consists of two pages [EQ-5 descriptive system and EQ Visual Analogue Scale (VAS)]. The EQ-5 descriptive system comprises five dimensions: mobility, self care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels: no problems, some problems, severe problems. The EQ-VAS records the respondent's self-rated health on a vertical VAS where the endpoints are labelled "Best imaginable health state" and "Worst imaginable health state"

ITT population

End point type	Secondary

End point timeframe:

Baseline and End-of-study Visit (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	50		
Units: Units on scale				
median (inter-quartile range (Q1-Q3))	-9 (-74 to 63)	-3.5 (-55 to 30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Profile of Tasquinimod

End point title	Safety Profile of Tasquinimod

End point description:

Number of subjects reporting adverse events

Safety Population: All patients who received at least one dose of study treatment. Patients were allocated to the treatment they actually received

End point type	Secondary

End point timeframe:

At regular intervals during the study treatment period and every 3 months during the follow-up until death (approximately up to 2.5 years)

End point values	Tasquinimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	70		
Units: Participants				
Any Treatment Emergent Adverse Event (TEAEs)	69	66		
Intensity of TEAEs [Grade 3-5 (severe)]	36	19		
Intensity of TEAEs [Grade 5]	1	3		
Intensity of TEAEs [Grade 4]	3	2		
Intensity of TEAEs [Grade 3]	32	14		
Intensity of TEAEs [Grade 2 (moderate)]	28	28		
Intensity of TEAEs [Grade 1 (mild)]	5	19		
Causality of TEAEs [Drug Related]	54	38		
Causality of TEAEs [Not Drug Related]	15	28		
TEAEs Leading to Drug Withdrawal	12	3		
TEAEs leading to Dose Reduction	16	2		
TEAEs leading to Drug Interruption	33	12		
TEAEs Leading to Death	1	0		
Serious Adverse Event (SAEs)	24	16		
Drug Related SAEs	6	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

At regular intervals during the study treatment period and every 3 months during the follow-up until death (approximately up to 2.5 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Tasquinimod

Reporting group description:

1 capsule daily, taken orally with water and food (0.25 mg initially then dose escalated to 0.5 mg and then to 1 mg per day) until disease progression.

Tasquinimod: Patients received initially an oral dose of 0.25 mg/day of tasquinimod, starting on Day 1, for at least 2 weeks. Once tolerability of the 0.25 mg/day dose was established, patients received a dose increase to 0.5 mg/day for at least 2 weeks, and then increased to 1 mg/day of study treatment. Patients showing poor tolerability for the escalated doses of tasquinimod were allowed to continue study treatment at the highest individually tolerated dose

Withdrawn during treatment period 59 (AE 13, Consent withdrawn 13, Disease progression 31, Other 2)

Reporting group title	Placebo

Reporting group description:

1 capsule daily, taken orally with water and food until disease progression

Placebo: Patients received Placebo capsules (identical to tasquinimod capsules) to be taken orally once a day with water and food.

Withdrawn during treatment period 61 (AE 3, Consent withdrawn 6, Disease progression 46, Other 6)

Serious adverse events	Tasquinimod	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Tasquinimod	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Details of SAE and common (incidence >5%) TEAEs has been attached as an appendix, since there are no occurence details available.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2013	• Change in Inclusion Criteria concerning the cumulative rather than starting dose of docetaxel and consideration of PSA measurements, including addition of a fourth measurement in certain circumstances. • Change in Exclusion Criterion by addition of history of venous thrombo embolic disease. • Clarification of statistical analysis. • A definition of visceral metastases has been added. • Tumour assessment follow-up for radiological progression has been clarified. • A list of disallowed foods were added due to their inhibitory effect on the activity of CYP 3A4. • Clarification of laboratory abnormalities that had to be reported as AEs. • Administrative changes, correction of typographical errors and alignment of sample collection times to be in accordance with the Schedule of Assessments.

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.

The study was terminated early due to the stop of the project as decided by sponsor. The trial included number of planned patients & number of events(PFS)were met to draw conclusions. Only follow-up of patients were discontinued earlier than planned.

Notes: