Clinical trial results:
Randomized phase III study comparing the association of hormone treatment + docetaxel with hormone treatment alone in metastatic prostate cancer

Summary

EudraCT number	2004-001984-22
Trial protocol	BE
Global end of trial date	15 December 2015

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	GETUG 15/0403

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00104715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Unicancer
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75013
Public contact	Nourredine AIT-RAHMOUNE, Unicancer, 33 1 71 93 67 04, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT-RAHMOUNE, Unicancer, 33 1 71 93 67 04, n.ait-rahmoune@unicancer.fr

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	15 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the GETUG15 study is to compare the 3-year overall survival (OS) of metastatic prostate cancers patients treated with first-line chemotherapy (docetaxel) + androgen deprivation therapy (ADT) to those treated only with ADT.

Protection of trial subjects:

In order to ensure the protection of the rights, safety and well-being of trial subjects, this clinical trial was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.
Furthermore, an independent Ethics Committees reviewed and gave a favorable opinion to the study documents, including the initial protocol and all subsequent amendments, and all information and documents provided to subjects/patients.
Written informed consent was obtained from all patients prior to enrollment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 October 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 383
Worldwide total number of subjects	385
EEA total number of subjects	385

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	216
From 65 to 84 years	169
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

GETUG 15 is a A multicentre, randomized, open-label phase III study was designed to evaluate the efficacy and safety of docetaxel combined with hormone therapy compared to hormone therapy alone in HSMPC. 385 patients were included form 18-Oct-2004 to 31-Dec-2008.

Pre-assignment

Screening details:

The study consisted of a screening phase of up to 30 days before treatment initiation to establish eligibility and document baseline measurements, a treatment phase (21-day cycle), and a long-term follow-up to monitor overall survival, clinical progression, quality of life, and safety.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Docetaxel plus hormone therapy

Arm description:

Patients were randomly allocated to receive Docetaxel once every 3 weeks until disease progression for a maximum of 9 cycles (1 cycle = 3 weeks).
The following hormone therapies were allowed during the study either:
* LHRH agonist (Zoladex®)
* Surgical castration
* Complete androgen blockage (CAB): combination of LHRH agonist (Zoladex®) and peripheral antiandrogen (Anandron®).
The hormone therapy started less than 2 months before docetaxel treatment initiation. The hormone treatment and docetaxel treatment could have been initiated at the same time. The hormone treatment was continued until androgen resistance.

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m²/day on day 1 of every 3 week cycle until disease progression for a maximum of 9 cycles

Investigational medicinal product name	Goserelin
Investigational medicinal product code	
Other name	Zoladex
Pharmaceutical forms	Implant in pre-filled syringe
Routes of administration	Implantation

Dosage and administration details:

3.6 mg implant goserelin started less than 2 months before Docetaxel treatment. The Goserelin and docetaxel could have been initiated at the same time. The goserelin treatment was continued until androgen resistance.

Investigational medicinal product name	Nilutamide
Investigational medicinal product code	
Other name	Anandron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients swallowed 2 tablets of 150 mg nilutalide per day during 4 weeks, then 1 tablet daily day therafter.
When prescribed, nilutalide was administrated in combination with goserelin.
Nilutamide treatment started less than 2 months before docetaxel treatment. The Nilutamide treatment and docetaxel treatment could have been initiated at the same time. The Nilutamide treatment was continued until androgen resistance.

Arm title	Hormone therapy

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Goserelin
Investigational medicinal product code	
Other name	Zoladex
Pharmaceutical forms	Implant in pre-filled syringe
Routes of administration	Implantation

Dosage and administration details:

3.6 mg implant goserelin started less than 2 months before Docetaxel treatment. The goserelin treatment was continued until androgen resistance.

Investigational medicinal product name	Nilutamide
Investigational medicinal product code	
Other name	Anandron
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients swallowed 2 tablets of 150 mg nilutalide per day during 4 weeks, then 1 tablet daily day therafter.
When prescribed, nilutalide was administrated in combination with goserelin. The Nilutamide treatment was continued until androgen resistance.

Number of subjects in period 1	Docetaxel plus hormone therapy	Hormone therapy
Started	192	193
Completed	104	105
Not completed	88	88
Death	88	88

Baseline characteristics

Reporting groups

Reporting group title	Docetaxel plus hormone therapy

Reporting group description:

Patients were randomly allocated to receive Docetaxel once every 3 weeks until disease progression for a maximum of 9 cycles (1 cycle = 3 weeks).
The following hormone therapies were allowed during the study either:
* LHRH agonist (Zoladex®)
* Surgical castration
* Complete androgen blockage (CAB): combination of LHRH agonist (Zoladex®) and peripheral antiandrogen (Anandron®).
The hormone therapy started less than 2 months before docetaxel treatment initiation. The hormone treatment and docetaxel treatment could have been initiated at the same time. The hormone treatment was continued until androgen resistance.

Reporting group title	Hormone therapy

Reporting group description: -

Reporting group values	Docetaxel plus hormone therapy	Hormone therapy	Total
Number of subjects	192	193	385
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)	113	103	216
From 65-84 years	79	90	169
85 years and over	0	0	0
Age continuous Units: years			
median	63	64	
full range (min-max)	46 to 79	43 to 84	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	192	193	385
Gleason score Units: Subjects			
2-6	19	15	34
7.	67	64	131
8-10	106	114	220
Treatment for local disease Units: Subjects			
Prostatectomy	33	25	58
Radiotherapy	36	33	69
ADT	19	15	34
CHemotherapy	2	0	2

None	102	120	222
Metastatic at diagnosis Units: Subjects			
Yes	129	147	276
No	63	46	109
Prognostic group Units: Subjects			
Good	95	96	191
Intermediate	54	57	111
Poor	43	40	83
Karnofsky index Units: Percentage			
median	100	100	
full range (min-max)	70 to 100	60 to 100	-
PSA level Units: mg/ml			
median	26.7	25.85	
full range (min-max)	0.05 to 2170	0.1 to 11900	-

End points

End points reporting groups

Reporting group title	Docetaxel plus hormone therapy

Reporting group description:

Patients were randomly allocated to receive Docetaxel once every 3 weeks until disease progression for a maximum of 9 cycles (1 cycle = 3 weeks).
The following hormone therapies were allowed during the study either:
* LHRH agonist (Zoladex®)
* Surgical castration
* Complete androgen blockage (CAB): combination of LHRH agonist (Zoladex®) and peripheral antiandrogen (Anandron®).
The hormone therapy started less than 2 months before docetaxel treatment initiation. The hormone treatment and docetaxel treatment could have been initiated at the same time. The hormone treatment was continued until androgen resistance.

Reporting group title	Hormone therapy

Reporting group description: -

Primary: 3-year Overall survival

End point title	3-year Overall survival

End point description:

The principal objective was to compare the benefit on overall survival at 36 months of docetaxel + androgen blockade at the first metastatic phase versus androgen blockade only.

End point type	Primary

End point timeframe:

Overall survival was defined as the number of patients being alive at least 36 months after randomization.

End point values	Docetaxel plus hormone therapy	Hormone therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	193		
Units: Percent of patients				
median (confidence interval 95%)	64.2 (57.5 to 71.6)	62.9 (56.3 to 70.3)		

Statistical analyses

Statistical analysis title	3-year overall survival
Comparison groups	Hormone therapy v Docetaxel plus hormone therapy

Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.955
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.36

Secondary: Clinical progression free survival

End point title	Clinical progression free survival

End point description:

The date of clinical progression was defined as the date of the first investigation (bone scintigraphy, pelvic scan or MRI, etc.) to show clinical progression. In the absence PSA level increase, clinical progression on scintigraphy was considered when one or several new lesions appeared. In patients with measurable lesions, clinical progression was defined using RECIST 1.0. In patients with bone lesions only, disease progression was defined as the appearance of one or more new bone lesions on bone scan.

End point type	Secondary

End point timeframe:

Tumor assessments were performed at baseline and every 3 months for the first 3.5 years then every 6 months until disease progression.

End point values	Docetaxel plus hormone therapy	Hormone therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	193		
Units: Percent of patients				
median (confidence interval 95%)	23.5 (20.5 to 31.9)	15.4 (12.5 to 19.8)		

Statistical analyses

Statistical analysis title	Clinical progression free survival
Comparison groups	Docetaxel plus hormone therapy v Hormone therapy
Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.94

Secondary: biological/laboratory progression free survival

End point title	biological/laboratory progression free survival

End point description:

The biological/laboratory progression was evaluated using two definitions:

Using the Prostate Working Group 1 definition:
* For subjects without a decrease in PSA levels, or with a decrease in PSA levels of <50%, progression was defined as a 25% increase from the nadir with a minimum increase in absolute value of 5 ng/mL. A progression was confirmed by a second sample.
* For subjects who had a response in PSA levels of >50% confirmed by a second sample 1 month later, progression was defined as an increase of >50% in relation to the nadir with a minimum increase in absolute value of 5 ng/mL. A progression was confirmed by a second sample.

Using the recommendations of the Prostate Working Group 2:
Increase in the PSA level of 25% with respect to nadir and with an absolute increase of ≥2 ng/mL:
* After 12 weeks for the patients whose PSA levels did not decrease or decreased <50%.
* For patients whose PSA levels decrease ≥50%.

End point type	Secondary

End point timeframe:

The survival without biological/laboratory progression was calculated from date of randomization until the date of biological/laboratory progression, or death of any cause.

End point values	Docetaxel plus hormone therapy	Hormone therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	193		
Units: Months				
median (confidence interval 95%)	22.4 (17.4 to 25.9)	12.4 (9.9 to 15.1)		

Statistical analyses

Statistical analysis title	Biological/laboratory progression-free survival
Comparison groups	Docetaxel plus hormone therapy v Hormone therapy
Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.88

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomization until 30 days after end of treatment (up to 6 years).

Adverse event reporting additional description:

For non-serious adverse events, the number of occurrences were not recorded, the number of patient affected were the only value available. Thus, the number of patient affected was entered in both "Subjects affected number" and "Occurrence all number" fields.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	8

Reporting groups

Reporting group title	Docetaxel plus hormone therapy

Reporting group description:

Patients were randomly allocated to receive Docetaxel once every 3 weeks until disease progression for a maximum of 9 cycles (1 cycle = 3 weeks).
The following hormone therapies were allowed during the study either:
* LHRH agonist (Zoladex®)
* Surgical castration
* Complete androgen blockage (CAB): combination of LHRH agonist (Zoladex®) and peripheral antiandrogen (Anandron®).
The hormone therapy started less than 2 months before docetaxel treatment initiation. The hormone treatment and docetaxel treatment could have been initiated at the same time. The hormone treatment was continued until androgen resistance.

Reporting group title	Hormone therapy

Reporting group description: -

Serious adverse events	Docetaxel plus hormone therapy	Hormone therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	76 / 189 (40.21%)	33 / 186 (17.74%)	
number of deaths (all causes)	88	88	
number of deaths resulting from adverse events	4	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of prostate			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell epithelioma			
subjects affected / exposed	0 / 189 (0.00%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung carcinoma			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer stage unspecified			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer metastatic			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Arterial insufficiency periferal			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Claudication intermittent			

subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke			
subjects affected / exposed	3 / 189 (1.59%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis arterial leg			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone operation			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrectomy			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rehabilitation therapy			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polypectomy			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal decompression			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent placement			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral repair			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Catheter site infection			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General discomfort			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	7 / 189 (3.70%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Injection site infection			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenocarcinoma lung			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exacerbated			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia interstitial			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic pain			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 189 (0.00%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Catheter sepsis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Compression fracture vertebra			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis injection site			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac insufficiency			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain retrosternal			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic pain			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac discomfort			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 189 (0.00%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Nervous system disorders			
Bleeding intracranial			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma non diabetic			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusion			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiduritis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy NOS			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vagal reaction			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile aplasia			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	6 / 189 (3.17%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	25 / 189 (13.23%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	39 / 39	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			

subjects affected / exposed	2 / 189 (1.06%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	2 / 2	0 / 0	
Gastrointestinal disorders			
Abdominal pain localised			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction NOS			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 189 (0.53%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis perforative			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin cancer			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis NOS			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis aggravated			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 189 (1.06%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macroscopic haematuria			

subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal insufficiency			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary obstruction unspecified			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 189 (1.06%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes mellitus insulin-dependent			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumbar pain			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in spine			
subjects affected / exposed	0 / 189 (0.00%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain lower ribs			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Polyarthritis			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 189 (0.53%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enzyme abnormality			
subjects affected / exposed	0 / 189 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Docetaxel plus hormone therapy	Hormone therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	189 / 189 (100.00%)	186 / 186 (100.00%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	140 / 189 (74.07%)	37 / 186 (19.89%)	
occurrences (all)	140	37	
Fever (in the abscence of neutropenia)			
subjects affected / exposed	20 / 189 (10.58%)	1 / 186 (0.54%)	
occurrences (all)	20	1	
Gain or loss of weight			
subjects affected / exposed	38 / 189 (20.11%)	21 / 186 (11.29%)	
occurrences (all)	38	21	

Hot flashes			
subjects affected / exposed	70 / 189 (37.04%)	118 / 186 (63.44%)	
occurrences (all)	70	118	
Pain			
subjects affected / exposed	32 / 189 (16.93%)	26 / 186 (13.98%)	
occurrences (all)	32	26	
Reproductive system and breast disorders			
Urinary tract infection			
subjects affected / exposed	21 / 189 (11.11%)	23 / 186 (12.37%)	
occurrences (all)	21	23	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	36 / 189 (19.05%)	3 / 186 (1.61%)	
occurrences (all)	36	3	
Cough			
subjects affected / exposed	26 / 189 (13.76%)	2 / 186 (1.08%)	
occurrences (all)	26	2	
Psychiatric disorders			
Libido decreased			
subjects affected / exposed	21 / 189 (11.11%)	28 / 186 (15.05%)	
occurrences (all)	21	28	
Cardiac disorders			
Oedema			
subjects affected / exposed	55 / 189 (29.10%)	10 / 186 (5.38%)	
occurrences (all)	55	10	
Nervous system disorders			
Sensory neuropathy			
subjects affected / exposed	54 / 189 (28.57%)	7 / 186 (3.76%)	
occurrences (all)	54	7	
Insomnia			
subjects affected / exposed	16 / 189 (8.47%)	8 / 186 (4.30%)	
occurrences (all)	16	8	
Blood and lymphatic system disorders			
Haemoglobin			
subjects affected / exposed	136 / 189 (71.96%)	41 / 186 (22.04%)	
occurrences (all)	136	41	
Neutrophils/granulocytes			

subjects affected / exposed	94 / 189 (49.74%)	5 / 186 (2.69%)	
occurrences (all)	94	5	
Platelet			
subjects affected / exposed	20 / 189 (10.58%)	9 / 186 (4.84%)	
occurrences (all)	20	9	
Gastrointestinal disorders			
Anorexia			
subjects affected / exposed	14 / 189 (7.41%)	1 / 186 (0.54%)	
occurrences (all)	14	1	
Constipation			
subjects affected / exposed	42 / 189 (22.22%)	9 / 186 (4.84%)	
occurrences (all)	42	9	
Diarrhoea			
subjects affected / exposed	58 / 189 (30.69%)	4 / 186 (2.15%)	
occurrences (all)	58	4	
Nausea			
subjects affected / exposed	55 / 189 (29.10%)	4 / 186 (2.15%)	
occurrences (all)	55	4	
Stomatitis/pharyngitis			
subjects affected / exposed	15 / 189 (7.94%)	0 / 186 (0.00%)	
occurrences (all)	15	0	
Vomiting			
subjects affected / exposed	16 / 189 (8.47%)	0 / 186 (0.00%)	
occurrences (all)	16	0	
Mucositis			
subjects affected / exposed	40 / 189 (21.16%)	0 / 186 (0.00%)	
occurrences (all)	40	0	
Hepatobiliary disorders			
Alkaline phosphatase			
subjects affected / exposed	52 / 189 (27.51%)	40 / 186 (21.51%)	
occurrences (all)	52	40	
Alanine aminotransferase			
subjects affected / exposed	43 / 189 (22.75%)	22 / 186 (11.83%)	
occurrences (all)	43	22	
Aspartate aminotransferase			

subjects affected / exposed	38 / 189 (20.11%)	17 / 186 (9.14%)	
occurrences (all)	38	17	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	102 / 189 (53.97%)	1 / 186 (0.54%)	
occurrences (all)	102	1	
Rash/desquamation			
subjects affected / exposed	29 / 189 (15.34%)	3 / 186 (1.61%)	
occurrences (all)	29	3	
Skin reaction/hands-feet			
subjects affected / exposed	27 / 189 (14.29%)	1 / 186 (0.54%)	
occurrences (all)	27	1	
Nail alert			
subjects affected / exposed	74 / 189 (39.15%)	0 / 186 (0.00%)	
occurrences (all)	74	0	
Renal and urinary disorders			
Creatinine			
subjects affected / exposed	21 / 189 (11.11%)	14 / 186 (7.53%)	
occurrences (all)	21	14	
Nycturia			
subjects affected / exposed	23 / 189 (12.17%)	17 / 186 (9.14%)	
occurrences (all)	23	17	
Endocrine disorders			
Gynecomastia			
subjects affected / exposed	8 / 189 (4.23%)	10 / 186 (5.38%)	
occurrences (all)	8	10	
Infections and infestations			
Febrile neutropenia			
subjects affected / exposed	15 / 189 (7.94%)	0 / 186 (0.00%)	
occurrences (all)	15	0	
Infection without neutropenia			
subjects affected / exposed	25 / 189 (13.23%)	3 / 186 (1.61%)	
occurrences (all)	25	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2004	The chemotherapy used in the study for Arm A was changed from docetaxel with estramustine to only docetaxel.
12 October 2005	G-CSF was administrated to patients in the experimental arm to prevent docetaxel-induced severe neutropenia. Following an increase in the frequency of thromboembolic events and abnormal death rates in other studies evaluating the use of growth factors in cancer patients. The French Competent authority and the EMEA demanded that the protocol and patient's information sheet be modified to take into account the new administration rules for Aranesp®.
06 July 2007	Following an IDMC and after the accrual of 215 subjects, 2 treatment-related deaths were reported in Arm A, due to neutropenic fever and pulmonary embolism. The independent data monitoring committee recommended the systematic administration of granulocytes colony-stimulating factors (G-CSF) from day 5 to day 10 at each docetaxel cycle.

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 investigators underestimated OS in the ADT group and overestimated potential difference in term of survival for the sample size calculation. Thus the study did not have sufficient power to show a small difference in OS.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23306100