Clinical trial results:
Personalized treatment of metastatic Castrate-resistant prostate cancer patients according to circulating tumor cells kinetic during chemotherapy

Summary

EudraCT number	2016-002429-12
Trial protocol	FR
Global end of trial date	26 August 2021

Results information

Result version number	v1 (current)
This version publication date	07 March 2025
First version publication date	07 March 2025

Trial information

Trial identification

Sponsor protocol code	UC_0160/1613

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03101046
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT RAHMOUNE, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT RAHMOUNE, UNICANCER, 33 0171936704, 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	05 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 August 2021
Global end of trial reached?	Yes
Global end of trial date	26 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the biological activity of cabazitaxel (6 cycles) to that of docetaxel (6 cycles) in metastatic castrate-resistant prostate cancer (mCRPC) patients with docetaxel resistant mCPRC defined as ≥ 5CTCs/7.5ml after 2 cycles of docetaxel.

Protection of trial subjects:

This study was conducted in compliance with the protocol described in Section 16.1.1, and in accordance with the French national regulatory requirements:
- Loi n°2012-300 du 5 mars 2012 (dite loi "Jardé ") relative aux recherches impliquant la personne humaine,
- Loi Informatique et Libertés n° 78-17 du 6 janvier 1978 modifiée, relative à la protection des personnes physiques à l'égard des traitements de données à caractère personnel,
- Loi n° 2004-800 du 6 août 2004 modifiée, relative à la bioéthique,
- Décision portant sur les Bonnes Pratiques Cliniques du 24 novembre 2006,
- Bonnes Pratiques de Fabrication en vigueur, notamment la ligne directrice 13, relative aux médicaments expérimentaux.
- Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	9
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 12 centres randomized 40 patients between March 08th, 2019 and October 14th, 2020, a period of inclusion of 19.3 months.

Pre-assignment

Screening details:

After signature of the consent form and assessment of the eligibility criteria, blood samples were collected from eligible patients. CTCs were enumerated using the CellSearch System (CTC count screening).
Patients with unfavorable CTC count at screening defined as ≥ 5 CTC/7.5 mL were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group I: Cohort

Arm description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel sensitive (<5 CTCs/7.5 mL) after 2 cycles of docetaxel. The patients will receive 6 additional cycles of docetaxel..

Arm type	Standard treatment arm and cohort
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel is administered at the dose of 75 mg/m² over 1 hour every 3 weeks for 6 cycles (D1=D22).

Arm title	Group II: Arm A

Arm description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel.
Patients will be randomized in Arm A and will receive 6 additional cycles of docetaxel (75 mg/m2 every 3 weeks) after randomization.

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel is administered at the dose of 75 mg/m² over 1 hour every 3 weeks for 6 cycles (D1=D22).

Arm title	Group II: Arm B

Arm description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel.

Patients will be randomized in Arm B and will receive 6 cycles of cabazitaxel (20 mg/m2 every 3 weeks) after randomization.

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

patients will be treated with intravenous cabazitaxel 20 mg/m2 every 3 weeks for 6 cycles (D1=D22).

Number of subjects in period 1	Group I: Cohort	Group II: Arm A	Group II: Arm B
Started	21	6	4
Completed	4	0	0
Not completed	17	6	4
Early termination requested by the sponsor	1	-	-
Promotor's decision	1	-	-
Early termination by the sponsor	1	-	-
Death	13	6	3
Promotor decision	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group I: Cohort
Reporting group description:	
Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel sensitive (<5 CTCs/7.5 mL) after 2 cycles of docetaxel. The patients will receive 6 additional cycles of docetaxel..	
Reporting group title	Group II: Arm A
Reporting group description:	
Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel. Patients will be randomized in Arm A and will receive 6 additional cycles of docetaxel (75 mg/m2 every 3 weeks) after randomization.	
Reporting group title	Group II: Arm B
Reporting group description:	
Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel. Patients will be randomized in Arm B and will receive 6 cycles of cabazitaxel (20 mg/m2 every 3 weeks) after randomization.	

Reporting group values	Group I: Cohort	Group II: Arm A	Group II: Arm B
Number of subjects	21	6	4
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)	5	3	1
From 65-84 years	16	3	3
85 years and over	0	0	0
Age continuous Units: years			
median	70	64.5	71
full range (min-max)	52 to 82	58 to 75	55 to 72
Gender categorical Units: Subjects			
Female	0	0	0
Male	21	6	4
ECOG Units: Subjects			
ECOG 0	9	2	0
ECOG 1	11	2	4
ECOG 2	1	2	0
Clinical exam Units: Subjects			

Normal	20	6	4
Abnormal	1	0	0

Reporting group values	Total		
Number of subjects	31		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	9		
From 65-84 years	22		
85 years and over	0		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	0		
Male	31		
ECOG Units: Subjects			
ECOG 0	11		
ECOG 1	17		
ECOG 2	3		
Clinical exam Units: Subjects			
Normal	30		
Abnormal	1		

End points

End points reporting groups

Reporting group title	Group I: Cohort

Reporting group description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel sensitive (<5 CTCs/7.5 mL) after 2 cycles of docetaxel. The patients will receive 6 additional cycles of docetaxel..

Reporting group title	Group II: Arm A

Reporting group description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel.
Patients will be randomized in Arm A and will receive 6 additional cycles of docetaxel (75 mg/m2 every 3 weeks) after randomization.

Reporting group title	Group II: Arm B

Reporting group description:

Patients with unfavorable CTC count (≥ 5 CTCs/7.5 mL) before initiation of docetaxel chemotherapy and subsequently docetaxel resistant (≥ 5 CTCs/7.5 mL) after 2 cycles of docetaxel.
Patients will be randomized in Arm B and will receive 6 cycles of cabazitaxel (20 mg/m2 every 3 weeks) after randomization.

Primary: Biological activity of chemotherapy

End point title	Biological activity of chemotherapy[1]

End point description:

Biological activity of chemotherapy was defined as < 5 CTCs per 7.5 mL at the end of chemotherapy with docetaxel or cabazitaxel (irrespective of the number of cycles received after the 2 cycles of docetaxel preceeding randomization). The CellSearch CTC Test (Janssen) was used to assess CTC.
Biological activity will be categorized as follows:
- Biological Activity: if < 5 CTCs per 7.5 mL are observed at the end of the treatment,
- Absence of biological activity: if ≥ 5 CTCs per 7.5 mL are observed at the end of the treatment.
- No interpretable results: CTC count performed at the end of the treatment but results not interpretable

End point type	Primary

End point timeframe:

18 weeks after randomisation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint was the biological activity of chemotherapy defined as < 5 CTCs per 7.5 mL at the end of chemotherapy with Docetaxel or Cabazitaxel (irrespective of the number of cycles received after the 2 cycles of docetaxel preceding randomization). In group I, there were 10 failures (47.6%) and 10 success (52.4%). In group II, there were 6 (100.0%) failures in arm A, and 2 (50.0%) success and 2 (50.0%) failures in arm B (p=0.133). There were no statistical comparisons between groups.

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: Number				
FAILURE	10	6	2	
SUCCESS	11	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Prostate Specific Antigen PSA progression-free-survival (PSA-PFS)

End point title	Prostate Specific Antigen PSA progression-free-survival (PSA-PFS)

End point description:

Prostate Specific Antigen -Progression Free Survival (PSA-PFS) is defined as the time from the date of randomization until first evidence of PSA progression or until death from any cause, whichever comes first. PSA progression is defined by the criteria of the Prostate Cancer Clinical Trials Working Group (PCWG 3) [1] as follows :
-For patients with a PSA decrease observed after baseline: PSA progression is defined as the first PSA increase that is ≥ 25% and ≥ 2 ng/mL above the nadir, and which is confirmed by a second value ≥ 3 weeks later. The date of progression corresponds to the date of the first PSA increase that is ≥ 25% and ≥ 2 ng/mL above the nadir.
-For patients without a PSA decrease observed after baseline: PSA progression is defined as PSA progression ≥ 25% increase and ≥ 2 ng/mL increase from baseline beyond 12 weeks.
-PSA value will be assessed at each cycle of chemotherapy.

End point type	Secondary

End point timeframe:

The time from the date of randomization until first evidence of PSA progression or until death from any cause, whichever comes first.

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: Months				
median (confidence interval 95%)	7.9 (3.6 to 9.2)	1.8 (0.7 to 6.4)	1.4 (1.4 to 4.0)	

Statistical analyses

Statistical analysis title	PSA-PFS Analysis
Comparison groups	Group II: Arm A v Group II: Arm B
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489
Method	Logrank

Secondary: Radiographic progression-free survival (rPFS)

End point title	Radiographic progression-free survival (rPFS)

End point description:

rPFS is defined as the time from the date of randomization to the date when the first site of disease is found to progress (using a manifestation-specific definition of progression), or death from any cause, whichever occurs first:
- Soft tissue: Radiographic progression is defined as an increase in measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1).
- Bone: Bone progression is defined by the occurrence of at least 2 new lesions.
- Imaging will be assessed at baseline, after 2 cycles, at the end of treatment and at any time whenever investigator considers it necessary..

End point type	Secondary

End point timeframe:

The time from the date of randomization to the date when the first site of disease is found to progress, or death from any cause, whichever occurs first

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: Months				
median (confidence interval 95%)	7.7 (3.8 to 9.1)	4.2 (1.5 to 8.5)	4.8 (4.0 to 13.5)	

Statistical analyses

Statistical analysis title	rPFS analysis
Comparison groups	Group II: Arm A v Group II: Arm B
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.425
Method	Logrank

Secondary: Time to pain progression

End point title	Time to pain progression

End point description:

Time to pain progression is defined as the time from the date of randomization to the first documentation of pain progression , as used by Bash et al.
- Progression of mean pain intensity (items 3 [worst pain], 4 [least], 5 [mean], and 6 [present]) was defined as a 30% increase from baseline* (increase necessary at two consecutive assessments at least 4 weeks apart without a decrease in WHO analgesic usage score).
- Evaluation of mean pain progression was based on the Short Form Brief Pain inventory.
- Analgesic use was scored according to WHO criteria: zero for no use, one for use of non-opiate analgesics (eg, nonsteroidal anti-inflammatory drugs, acetaminophen, antidepressants, and agents targeting neuropathic pain), two for use of weak opiates for moderate pain (eg,codeine and tramadol), and three for strong opiates for severe pain (eg, morphine and fentanyl).
- Pain and analgesic use as per WHO was assessed every 2 cycles of chemotherapy, as well at treatment discontinuation

End point type	Secondary
End point timeframe: at 1 year after randomization	

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: percent				
number (confidence interval 95%)	5.1 (0.3 to 21.3)	16.7 (0.5 to 54.9)	0 (0 to 0)	

Statistical analyses

Statistical analysis title	Time to pain progression Analysis
Comparison groups	Group II: Arm A v Group II: Arm B
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.291
Method	Gray test

Secondary: Disease Specific Survival (DSS)	
End point title	Disease Specific Survival (DSS)
End point description: DSS was defined as the time from the date of randomization to the date of prostate cancer death.	
End point type	Secondary
End point timeframe: at 1 year after randomization	

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: percent				
number (not applicable)	41.8	83.3	50.0	

Statistical analyses

Statistical analysis title	DSS Anlaysis
Comparison groups	Group II: Arm A v Group II: Arm B
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.282
Method	Gray test

Secondary: Overall survival (OS)	
End point title	Overall survival (OS)
End point description: OS was defined as the time from the date of randomization to the date of death from any cause. Note:	
End point type	Secondary
End point timeframe: The time from the date of randomization to the date of death from any cause.	

End point values	Group I: Cohort	Group II: Arm A	Group II: Arm B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	6	4	
Units: Median (months)				
number (not applicable)	12.5	8.1	4.4	

Statistical analyses

Statistical analysis title	OS analysis
Comparison groups	Group II: Arm A v Group II: Arm B
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.784
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of the informed consent form up to 30 days after the post-treatment CTC sample performed 4 weeks after the last cycle of the study treatment (docetaxel or cabazitaxel).

Adverse event reporting additional description:

Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Group I
Reporting group description: -	
Reporting group title	Group II: Arm A
Reporting group description: -	
Reporting group title	Group II: Arm B

Reporting group description: -

Serious adverse events	Group I	Group II: Arm A	Group II: Arm B
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 21 (33.33%)	3 / 6 (50.00%)	3 / 4 (75.00%)
number of deaths (all causes)	13	6	3
number of deaths resulting from adverse events	0	0	1
Cardiac disorders			
Pulmonary oedema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplasia bone marrow			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Febrile aplasia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Macrophage activation syndrome			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ulcerative duodenitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic cytolysis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumopathy			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Acute renal insufficiency			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cholecystitis infective			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septicemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

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

Non-serious adverse events	Group I	Group II: Arm A	Group II: Arm B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	6 / 6 (100.00%)	4 / 4 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Hypotension			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Painful hematoma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Varicose ulceration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Thromboembolic event			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Varicose vein			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Aches			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Anasarca			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Costal pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Oedema limbs			
subjects affected / exposed	5 / 21 (23.81%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	12	0	0
Extravasation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Face edema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	21 / 21 (100.00%)	6 / 6 (100.00%)	4 / 4 (100.00%)
occurrences (all)	86	33	24
Fever			
subjects affected / exposed	1 / 21 (4.76%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Gait disturbance			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
General physical health deterioration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1
Hip pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperthermia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oedema lower limb			
subjects affected / exposed	7 / 21 (33.33%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	14	0	4
Infusion site extravasation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	3
Mucositis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Mucositis oral			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	2
Edema			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Edema limb			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	4	0
Chest pain			

subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	4	0
Thoracic pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Throat pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Xerosis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	3	5	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	7	5
Penile irritation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	5 / 21 (23.81%)	1 / 6 (16.67%)	3 / 4 (75.00%)
occurrences (all)	5	2	6
Epistaxis			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Rhinorrhea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Voice alteration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Depression			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Depressive syndrom			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	5	0	1
Hallucination			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Libido decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	5
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Alkaline phosphatase increased			
subjects affected / exposed	4 / 21 (19.05%)	3 / 6 (50.00%)	4 / 4 (100.00%)
occurrences (all)	8	6	10
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	3	1	4
Blood lactate dehydrogenase			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Creatinine increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 21 (14.29%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	4	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hematuria			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Hypocalcemia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	4	0	2
Hyponatraemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Blood phosphorus decreased			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	7	0	4
Neutrophil count decreased			
subjects affected / exposed	3 / 21 (14.29%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	4	5	2
Platelet count decreased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	3 / 4 (75.00%)
occurrences (all)	1	2	11
Weight gain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Weight loss			
subjects affected / exposed	13 / 21 (61.90%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	32	1	5
White blood cell count decreased			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	3	0	1
Injury, poisoning and procedural complications			
Chemical phlebitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cardiac arrhythmia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cardiac decompensation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Palpitations			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tricuspid insufficiency			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	7 / 21 (33.33%)	0 / 6 (0.00%)	4 / 4 (100.00%)
occurrences (all)	9	0	14
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Drowsiness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypoesthesia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Memory loss			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	8	0
Metal taste in mouth			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Paresthesia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	10 / 21 (47.62%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	30	5	6

Presyncope			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Radicular pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	8	0	1
Head pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	12 / 21 (57.14%)	4 / 6 (66.67%)	4 / 4 (100.00%)
occurrences (all)	66	26	30
Febrile neutropenia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Watering			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
Eye disorders			
Acuity visual loss			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Convergent strabismus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye tearing			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Lacrimation disorder			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Myosis/Ptosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	2 / 6 (33.33%)	2 / 4 (50.00%)
occurrences (all)	2	2	4
Bleeding ulcer			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	5 / 21 (23.81%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	6	0	1
Diarrhea			
subjects affected / exposed	15 / 21 (71.43%)	3 / 6 (50.00%)	3 / 4 (75.00%)
occurrences (all)	35	3	10
Digestive disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Hemorrhoids			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hiatal hernia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Nausea			
subjects affected / exposed	10 / 21 (47.62%)	2 / 6 (33.33%)	2 / 4 (50.00%)
occurrences (all)	13	5	3
Pyrosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Proctitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rectorrhage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Gastric pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Thrombosed hemorrhoids			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	6 / 21 (28.57%)	2 / 6 (33.33%)	4 / 4 (100.00%)
occurrences (all)	8	3	4
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 21 (38.10%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	31	2	5
Cutaneous lesion			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	11	0	0
Erythema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hand and foot syndrome			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nail disorder			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	13	1	0
Nail toxicity			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
Night sweats			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Onychodystrophy			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Onychopathia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Onycholysis			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Peripheral rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Rash at injection site			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Redness			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin pallor			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute renal failure			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dilatation of left urinary cavities			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Urinary incontinence			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Partial urinary retention			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal insufficiency			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urethral obstruction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary disorder			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Asthenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	16	0	0
Groin pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	5
Bone pain			
subjects affected / exposed	5 / 21 (23.81%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	5	0	2
Cervical pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Cramps in the calves			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dorsal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Femoral pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Generalised muscle weakness			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Knee pain			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	8	0	2
Femur pain			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sacroiliac pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lumbar pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	2	3	2
Muscle weakness			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	5 / 21 (23.81%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	16	0	0
Osteonecrosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Sacral pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sarcopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Scapula pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Shoulder pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Glans mycosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neoplasic meningitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oral mycosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Paronychia			
subjects affected / exposed	5 / 21 (23.81%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	14	0	0
Sepsis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Tooth abscess			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	8 / 21 (38.10%)	3 / 6 (50.00%)	4 / 4 (100.00%)
occurrences (all)	12	10	11
Dehydration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypercalcemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	3	1	2
Hypouricaemia			

subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2018	- Safety measures regarding the administration of docetaxel - Alignment of secondary endpoints and evaluation criteria for the duration of treatment - Update of secondary endpoints - Clarification of information on the processing of personal data - Update of the investigators list
08 March 2019	Update of the investigators list
03 October 2019	Update of the investigators list
27 November 2019	Update of the investigators list
04 February 2020	Update of the investigators list
02 September 2020	- Addition of a test to monitor heart function before starting treatment - Reformulation of the assessment methods for the secondary endpoints regarding to time to pain progression - Correction and precision regarding the frequency of tumour evaluation by imaging using RECIST v1.1 - Update on participant rights according to data protection regulation law - Withdrawal of the Oscar Lambret centre - Lilles
07 June 2021	- Prematurely discontinuation of the study due to poor recruitment of participants - Addendum on participant rights according to data protection regulation law

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 June 2021	Prematurely discontinuation of the study due to poor recruitment of participants, since enrolment opened in December 2018, only 40 patients with CTC count ≥5 /7.5 mL were included.	-

Notes:

Limitations and caveats

None reported