Clinical trial results:
A Phase 1-2 Dose Finding, Safety and Efficacy Study of Cabazitaxel in Pediatric Patients with Refractory Solid Tumors including Tumors of the Central Nervous System

Summary

EudraCT number	2015-002184-42
Trial protocol	Outside EU/EEA
Global end of trial date	18 February 2016

Results information

Result version number	v1 (current)
This version publication date	01 September 2016
First version publication date	01 September 2016

Trial information

Trial identification

Sponsor protocol code	TED12689

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01751308
WHO universal trial number (UTN)	U1111-1128-5704

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2015
Global end of trial reached?	Yes
Global end of trial date	18 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objectives: Phase 1 Part: To determine the dose limiting toxicity (DLT) and the maximum tolerated dose (MTD) of cabazitaxel as a single agent in pediatric subjects with recurrent or refractory solid tumors including tumors of the central nervous system. Phase 2 Part:
To determine the objective response rate (complete and partial response) and the duration of response to cabazitaxel as a single agent in subjects with recurrent or refractory high grade glioma (HGG) or diffuse intrinsic pontine glioma (DIPG).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric patients. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	39
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	26
Adolescents (12-17 years)	12
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 12 centres between February 2013 and March 2015.

Pre-assignment

Screening details:

Phase I was a dose escalation part to determine MTD of Cabazitaxel. Phase 2 was an efficacy and safety evaluation of Cabazitaxel at the MTD, determined in Phase 1. Disease progression (DP), adverse event (AE) and death were considered as completed (defined in protocol).

Period 1

Period 1 title	Phase 1 and Phase 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: Cabazitaxel 20 mg/m^2

Arm description:

Cabazitaxel 20 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel 20mg/m^2 IV infusion over 1 hour on Day 1 of each 21 -day cycle.

Arm title	Phase 1: Cabazitaxel 25 mg/m^2

Arm description:

Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel 25mg/m^2 IV infusion over 1 hour on Day 1 of each 21 -day cycle.

Arm title	Phase 1: Cabazitaxel 30 mg/m^2

Arm description:

Cabazitaxel 30 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Arm type	Experimental

Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel 30mg/m^2 IV infusion over 1 hour on Day 1 of each 21 -day cycle.

Arm title	Phase 1: Cabazitaxel 35 mg/m^2

Arm description:

Cabazitaxel 35 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel 35mg/m^2 IV infusion over 1 hour on Day 1 of each 21 -day cycle.

Arm title	Phase 2: Cabazitaxel 30 mg/m^2

Arm description:

Cabazitaxel at the MTD determined in phase 1 (30 mg/m^2) IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel at 30mg/m^2 IV infusion over 1 hour on Day 1 of each 21-day cycle.

Number of subjects in period 1	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2
Started	6	3	7
Completed	6	3	7

Number of subjects in period 1	Phase 1: Cabazitaxel 35 mg/m^2	Phase 2: Cabazitaxel 30 mg/m^2
Started	7	16
Completed	7	16

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: Cabazitaxel 20 mg/m^2
Reporting group description:	
Cabazitaxel 20 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 25 mg/m^2
Reporting group description:	
Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 30 mg/m^2
Reporting group description:	
Cabazitaxel 30 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 35 mg/m^2
Reporting group description:	
Cabazitaxel 35 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 2: Cabazitaxel 30 mg/m^2
Reporting group description:	
Cabazitaxel at the MTD determined in phase 1 (30 mg/m^2) IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	

Reporting group values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2
Number of subjects	6	3	7
Age categorical Units: Subjects			
2-4 years	0	0	2
5-6 years	2	1	0
7-11 years	1	1	3
12-18 years	3	1	2
Gender, Male/Female Units: subjects			
Female	5	0	1
Male	1	3	6

Reporting group values	Phase 1: Cabazitaxel 35 mg/m^2	Phase 2: Cabazitaxel 30 mg/m^2	Total
Number of subjects	7	16	39
Age categorical Units: Subjects			
2-4 years	0	2	4
5-6 years	1	4	8
7-11 years	5	4	14
12-18 years	1	6	13
Gender, Male/Female Units: subjects			
Female	2	8	16
Male	5	8	23

End points

End points reporting groups

Reporting group title	Phase 1: Cabazitaxel 20 mg/m^2
Reporting group description:	
Cabazitaxel 20 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 25 mg/m^2
Reporting group description:	
Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 30 mg/m^2
Reporting group description:	
Cabazitaxel 30 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 1: Cabazitaxel 35 mg/m^2
Reporting group description:	
Cabazitaxel 35 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Reporting group title	Phase 2: Cabazitaxel 30 mg/m^2
Reporting group description:	
Cabazitaxel at the MTD determined in phase 1 (30 mg/m^2) IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Subject analysis set title	Phase 1: Overall Population
Subject analysis set type	Full analysis
Subject analysis set description:	
Cabazitaxel 20 mg/m^2, 25 mg/m^2, 30 mg/m^2 or 35 mg/m^2 IV infusion on Day 1 of every 21-day cycle until DP or discontinuation due to AE or death (from any cause).	
Subject analysis set title	Phase 1 and 2: Cabazitaxel 30 mg/m^2
Subject analysis set type	Per protocol
Subject analysis set description:	
Cabazitaxel 30 mg/m^2 IV infusion on Day 1 of every 21-day cycle (at the MTD dose determined in Phase 1) in Phase 1 and Phase 2 until DP or death (from any cause).	

Primary: Phase 1: MTD of Cabazitaxel

End point title	Phase 1: MTD of Cabazitaxel[1]
End point description:	
MTD: highest dose level of cabazitaxel at which no more than 1 of 6 evaluable subjects experienced dose limiting toxicities (DLT). DLT: AE/abnormal laboratory values related to treatment: hematologic DLTs: Grade(G)4 hematologic toxicity except neutropenia G4 lasting≤7 days,G3/4 febrile neutropenia except in absence of granulocytecolony stimulating factor prophylaxis, G4thrombocytopenia; nonhematologic DLTs: G≥3 nonhematologic toxicity except G3 nausea/ G3/4 vomiting, G3/4 diarrhea,dehydration,G3 fatigue lasting≤7 days, hypersensitivity reactions, elevated transaminases<10*ULN of ≤7 days, retreatment delay of>2 weeks due to delayed recovery from toxicity related to study treatment to baseline G or≤ G1(except for alopecia) and platelet transfusion during Cycle1. Grades from NCICTCAE v4.0. DLT evaluable population: subset of subjects in Phase 1 part from all treated population who received first dose of cabazitaxel, had sufficient safety evaluations or experienced a DLT during Cycle 1.	
End point type	Primary
End point timeframe:	
Cycle 1 (21 days)	

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Phase 1: Overall Population			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: mg/m^2				
number (not applicable)	30			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Percentage of Subjects With Objective Response (OR)

End point title	Phase 2: Percentage of Subjects With Objective Response

End point description:

OR in subjects was defined as the subjects with a Complete Response (CR) or Partial Response (PR) after 3 cycles of cabazitaxel treatment and maintained for at least 4 weeks. CR and PR were based on the modified response assessment in neuro-oncology (RANO) criteria for subjects with CNS tumors. CR was defined as disappearance of all target lesions. PR was defined as ≥50% decrease in the sum of the products of the two perpendicular diameters of target lesions, compared to the baseline measurement. Efficacy evaluable population was the subset of all treated (AT) subjects with measurable disease with a baseline and at least one postbaseline tumor evaluation. Number of subjects analysed=subjects with available data for this endpoint.

End point type	Primary

End point timeframe:

Baseline, every 9 weeks until DP or death due to any cause (maximum duration: 12.1 weeks)

Notes:

[2] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for Phase 2 only.

End point values	Phase 2: Cabazitaxel 30 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percentage of subjects				
number (not applicable)				
CR	0			
PR	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR)[4][5]

End point description:

DOR defined as time (in days) from date of first response until date of first documented progressive disease (PD) or death (from any cause), whichever came first. If progression or death was not observed, subject was censored at the date of subject's last progression-free tumor assessment prior to study cut-off date. PD as per RANO criteria is defined as ≥ 25% increase in the product of perpendicular diameters of any target lesion, taking as reference the smallest product observed since the start of treatment or the appearance of one or more new lesions, or worsening neurologic status not explained by causes unrelated to tumor progression (example, anticonvulsant or corticosteroid toxicity, electrolyte disturbances, sepsis, hyperglycemia, presumed post-therapy swelling etc.) plus any increase in tumor cross-sectional area (or tumor volume).

End point type	Primary

End point timeframe:

Baseline, every 9 weeks until DP or death due to any cause (maximum duration: 12.1 weeks)

Notes:

[4] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for Phase 2 only.

End point values	Phase 2: Cabazitaxel 30 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[6] - Due to no objective responses in Stage 1 of Phase 2, analysis of DOR was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Phase 1 and 2: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

AE was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily have a causal relationship with the treatment. TEAEs were defined as AEs that developed or worsened during the on-treatment period which was defined as the period from the time of first dose of cabazitaxel until 30 days following the last administration of cabazitaxel. Analysis was performed on safety population (AT population).

End point type	Secondary

End point timeframe:

Baseline up to DP or death due to any cause (maximum duration: 112.1 weeks for Phase 1 and 12.1 weeks for Phase 2)

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	7	7
Units: subjects				
number (not applicable)	6	3	7	7

End point values	Phase 2: Cabazitaxel 30 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: subjects				
number (not applicable)	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Number of Subjects With Objective Response

End point title	Phase 1: Number of Subjects With Objective Response[7]

End point description:

OR in subjects was defined as the subjects with a CR or PR after 3 cycles of cabazitaxel treatment and maintained for at least 4 weeks as assessed by response evaluation criteria in solid tumors (RECIST) version 1.1 and RANO criteria for CNS tumors. For solid tumors, as per RECIST 1.1, CR defined as disappearance of all target and non-target lesions (any pathological lymph nodes, must have reduction in short axis to <10 mm); PR defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. For CNS tumors, as per RANO criteria, CR defined as disappearance of all target and non-target lesions; PR defined as a ≥50% decrease in the sum of the products of the two perpendicular diameters of target lesions, compared to baseline measurement. Analysis was performed on efficacy evaluable population. Number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks until DP or death due to any cause (maximum duration: 112.1 weeks)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for Phase 1 only.

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	7	7
Units: Subjects				
number (not applicable)	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2: Pharmacokinetics (PK) Parameter of Cabazitaxel: Area Under the Plasma Concentration (AUC) Versus Time Curve

End point title	Phase 1 and 2: Pharmacokinetics (PK) Parameter of Cabazitaxel: Area Under the Plasma Concentration (AUC) Versus Time Curve[8]

End point description:

Blood samples for PK parameters were collected at 5 minutes before end of infusion (EOI), 10 minutes, 30 minutes, 3 hours, 7 hours and 71 hours after the EOI on Day 1 of Cycle 1. PK population (for both Phase 1 and Phase 2 parts of the study) included all subjects who received treatment on Day 1 of Cycle 1 and had at least one post-dose PK sample. Number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI up to 71 hours after the EOI

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK data was reported for the combined population of Phase 1 and 2 at the MTD dose level.

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2	Phase 1 and 2: Cabazitaxel 30 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	3	2	20
Units: ng.h/mL				
arithmetic mean (standard deviation)	669.5 (± 430.6)	879 (± 414.7)	1002.5 (± 277.9)	876.7 (± 359.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2: PK Parameter of Cabazitaxel: Total Plasma Clearance (CL)

End point title	Phase 1 and 2: PK Parameter of Cabazitaxel: Total Plasma Clearance (CL)[9]

End point description:

Blood samples for PK parameters were collected at 5 minutes before EOI, 10 minutes, 30 minutes, 3 hours, 7 hours and 71 hours after the EOI on Day 1 of Cycle 1. Analysis was performed on PK population (for both Phase 1 and Phase 2 parts of the study). Number of subjects analysed =subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI up to 71 hours after the EOI.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK data was reported for the combined population of Phase 1 and 2 at the MTD dose level.

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2	Phase 1 and 2: Cabazitaxel 30 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	3	2	20
Units: L/h/m^2				
arithmetic mean (standard deviation)	36.05 (± 12.91)	32.76 (± 12.72)	36.61 (± 9.98)	38.7 (± 12.98)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2: PK Parameter of Cabazitaxel: Volume of Distribution at Steady State (Vss)

End point title	Phase 1 and 2: PK Parameter of Cabazitaxel: Volume of Distribution at Steady State (Vss)[10]

End point description:

Blood samples for PK parameters were collected at 5 minutes before EOI, 10 minutes, 30 minutes, 3 hours, 7 hours and 71 hours after the EOI on Day 1 of Cycle 1. Analysis was performed on PK population (for both Phase 1 and Phase 2 parts of the study). Number of
subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI up to 71 hours after the EOI

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK data was reported for the combined population of Phase 1 and 2 at the MTD dose level.

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2	Phase 1 and 2: Cabazitaxel 30 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	3	2	20
Units: L/m^2				
arithmetic mean (standard deviation)	3391.72 (± 686.79)	3301.96 (± 351.55)	1488.75 (± 1179.11)	3371.3 (± 975.98)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2: PK Parameter of Cabazitaxel: Maximum Plasma Concentration Observed (Cmax)

End point title	Phase 1 and 2: PK Parameter of Cabazitaxel: Maximum Plasma Concentration Observed (Cmax)[11]

End point description:

Blood samples for PK parameters were collected at 5 minutes before EOI, 10 minutes, 30 minutes, 3 hours, 7 hours and 71 hours after the EOI on Day 1 of Cycle 1. Analysis was performed on PK population (for both Phase 1 and Phase 2 parts of the study). Number of

subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI up to 71 hours after the EOI

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK data was reported for the combined population of Phase 1 and 2 at the MTD dose level.

End point values	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 35 mg/m^2	Phase 1 and 2: Cabazitaxel 30 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	3	2	20
Units: ng/mL				
arithmetic mean (standard deviation)	204.864 (± 189.864)	283.657 (± 242.97)	233.29 (± 0.127)	256.734 (± 127.931)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression Free Survival (PFS)

End point title	Phase 2: Progression Free Survival (PFS)[12]

End point description:

PFS: time (in months) from date of first dose administration until date of first documented PD or death (from any cause), whichever came first. If progression/death was not observed, the subject was censored at the date of subject's last progression-free tumor assessment prior to study cut-off date. PD as per RANO criteria defined as ≥ 25% increase in product of perpendicular diameters of any target lesion, taking as reference smallest product observed since start of treatment or appearance of one or more new lesions, or worsening neurologic status not explained by causes unrelated to tumor progression (example, anticonvulsant or corticosteroid toxicity, electrolyte disturbances, sepsis, hyperglycemia, presumed post-therapy swelling etc) plus any increase in tumor cross-sectional area (or tumor volume).The analysis was performed by Kaplan- Meier method. Analysis was performed on efficacy evaluable population. Number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks until DP or death due to any cause (maximum duration: 12.1 weeks)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for Phase 2 only.

End point values	Phase 2: Cabazitaxel 30 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: months				
median (confidence interval 95%)	1.3 (0.6 to 2.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)[13]

End point description:

OS was defined as the time (in months) from the date of first dose administration until the date of death (from any cause). If death was not observed, the subject was censored at the earliest of the last date the subject was known to be alive and the study cut-off date. The analysis was performed by Kaplan--Meier method. Analysis was performed on efficacy evaluable population. Number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to death or study cut-off (maximum duration: 12.1 weeks)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for phase 2 only.

End point values	Phase 2: Cabazitaxel 30 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: months				
median (confidence interval 95%)	2.7 (1.7 to 4.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from signature of the informed consent form up to the final visit (112.1 weeks for Phase 1 and 12.1 weeks for Phase 2) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are TEAEs that is AEs that developed/worsened during 'on treatment period' (time from first dose of study drug to last dose of study drug + 30 days). Analysis was performed on the safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Phase 1: Cabazitaxel 20 mg/m^2

Reporting group description:

Cabazitaxel 20 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Reporting group title	Phase 1: Cabazitaxel 25 mg/m^2

Reporting group description:

Cabazitaxel 25 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Reporting group title	Phase 1: Cabazitaxel 30 mg/m^2

Reporting group description:

Cabazitaxel 30 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Reporting group title	Phase 1: Cabazitaxel 35 mg/m^2

Reporting group description:

Cabazitaxel 35 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Reporting group title	Phase 2: Cabazitaxel 30 mg/m^2

Reporting group description:

Cabazitaxel at the MTD as determined in Phase 1 (30 mg/m^2) IV infusion on Day 1 of each 21-day cycle until DP or discontinuation due to AE or death (from any cause).

Serious adverse events	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	5 / 7 (71.43%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial Tumour Haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neoplasm Progression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease Progression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (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
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoventilation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain Herniation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Nerve Root Compression			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis Noninfective			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (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
Musculoskeletal and connective tissue disorders			
Bone Pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (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
Neutropenic Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma Site Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1: Cabazitaxel 35 mg/m^2	Phase 2: Cabazitaxel 30 mg/m^2	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)	12 / 16 (75.00%)	
number of deaths (all causes)	0	5	
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial Tumour Haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Progression			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease Progression			
subjects affected / exposed	0 / 7 (0.00%)	3 / 16 (18.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Death			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic Reaction			

subjects affected / exposed	0 / 7 (0.00%)	3 / 16 (18.75%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoventilation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Platelet Count Decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Brain Herniation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Cardiac Arrest			

subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nerve Root Compression			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	2 / 7 (28.57%)	3 / 16 (18.75%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	2 / 16 (12.50%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Cystitis Noninfective			

subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma Site Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase 1: Cabazitaxel 20 mg/m^2	Phase 1: Cabazitaxel 25 mg/m^2	Phase 1: Cabazitaxel 30 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter Site Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Localised Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gait Disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	2 / 7 (28.57%)
occurrences (all)	2	2	2
Device Occlusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Oedema Peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 3 (66.67%)	3 / 7 (42.86%)
occurrences (all)	0	3	4
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspnoea Exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Nasal Congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Oropharyngeal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pulmonary Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rhinitis Allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Confusional State			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Deja Vu			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Coronavirus Test Positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Candida Test Positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
White Blood Cell Count Decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Platelet Count Decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Injury, poisoning and procedural complications			
Rectal Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infusion Related Reaction			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Sinus Tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Sinus Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nervous system disorders			
Accessory Nerve Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Balance Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cerebellar Syndrome			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cerebellar Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cranial Nerve Paralysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Facial Nerve Disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	5	1	3
Hemiparesis			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Hydrocephalus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypotonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoglossal Nerve Disorder			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscle Spasticity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Viiith Nerve Lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vith Nerve Paralysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vith Nerve Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 7 (28.57%)
occurrences (all)	1	8	2

Eye disorders			
Cataract			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eyelid Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vision Blurred			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Abdominal Pain Upper			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	4 / 7 (57.14%)
occurrences (all)	2	3	4
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Dry Mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	3 / 7 (42.86%)
occurrences (all)	3	2	5
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	2 / 3 (66.67%)	3 / 7 (42.86%)
occurrences (all)	0	3	3
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Dry Skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin Ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Urinary Retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	3
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Bone Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Neck Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Joint Hyperextension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscular Weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Myalgia			

subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Pain In Extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	5
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Candida Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Enterocolitis Bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Lip Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Mucosal Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Non-serious adverse events	Phase 1: Cabazitaxel 35 mg/m^2	Phase 2: Cabazitaxel 30 mg/m^2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	15 / 16 (93.75%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Catheter Site Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Localised Oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gait Disturbance			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	3 / 7 (42.86%)	3 / 16 (18.75%)	
occurrences (all)	4	3	

Device Occlusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Oedema Peripheral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 16 (12.50%)	
occurrences (all)	2	2	
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dysmenorrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	

Atelectasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Aspiration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dyspnoea Exertional			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Nasal Congestion			
subjects affected / exposed	1 / 7 (14.29%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Oropharyngeal Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pulmonary Oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

Rhinitis Allergic			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Confusional State			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Deja Vu			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Investigations			
Coronavirus Test Positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Candida Test Positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Alanine Aminotransferase Increased			

subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Weight Decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Platelet Count Decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Rectal Injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Infusion Related Reaction			
subjects affected / exposed	2 / 7 (28.57%)	2 / 16 (12.50%)	
occurrences (all)	2	3	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Sinus Tachycardia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Sinus Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Accessory Nerve Disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Balance Disorder			

subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cerebellar Syndrome			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Cerebellar Ataxia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Ataxia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 16 (12.50%)	
occurrences (all)	2	2	
Dysarthria			
subjects affected / exposed	0 / 7 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Cranial Nerve Paralysis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	2 / 7 (28.57%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Facial Nerve Disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	2 / 7 (28.57%)	4 / 16 (25.00%)	
occurrences (all)	3	5	
Hemiparesis			
subjects affected / exposed	0 / 7 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Hydrocephalus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Hypotonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Lethargy			

subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Hypoglossal Nerve Disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Seizure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscle Spasticity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Viiith Nerve Lesion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Vith Nerve Paralysis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Vith Nerve Disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Eyelid Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Vision Blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Eye Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 7 (42.86%)	2 / 16 (12.50%)	
occurrences (all)	3	2	
Abdominal Pain Upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	5 / 16 (31.25%)	
occurrences (all)	1	6	
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	3 / 16 (18.75%)	
occurrences (all)	2	3	
Dry Mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dysphagia			

subjects affected / exposed	0 / 7 (0.00%)	6 / 16 (37.50%)	
occurrences (all)	0	6	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Ileus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Glossodynia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 7 (28.57%)	5 / 16 (31.25%)	
occurrences (all)	2	5	
Vomiting			
subjects affected / exposed	2 / 7 (28.57%)	4 / 16 (25.00%)	
occurrences (all)	2	4	
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dry Skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Skin Ulcer			

subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Urinary Retention			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Bone Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Neck Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Joint Hyperextension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscular Weakness			

subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pain In Extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Candida Infection			
subjects affected / exposed	0 / 7 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Enterocolitis Bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Lip Infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Mucosal Infection			
subjects affected / exposed	1 / 7 (14.29%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Varicella Zoster Virus Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Urinary Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased Appetite			

subjects affected / exposed	2 / 7 (28.57%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2012	- Exclusion criterion 9 changed to allow subjects being treated with continuous daily dexamethasone into the study, based on results from TCD10870 study indicating that CYP3A inducers have a limited impact on the PK of cabazitaxel. - Clarification of timing for: coagulation, ECG assessments, end of treatment visit, PK sampling, and granulocyte-colony stimulating factor (G-CSF) administration.
30 July 2013	- Phase 2 part (efficacy) was added to allow the study of HGG and DIPG patients in the safety expansion portion of Phase 1 with its integration into Stage 1 of Phase 2 thus reducing the exposure of subjects with non-CNS malignancies expected to benefit less from cabazitaxel treatment. - Enrollment opened for children 2-4 years old in Phase 1 part. - Addition of optional cerebrospinal fluid (CSF) collection. - Clarification of: reporting timelines, DLT definition, inclusion and exclusion criteria and PK analysis parameters.
31 January 2014	- The DLT definition was changed to avoid underreporting of thrombocytopenia as DLT. - Clarification of: dose escalation rules, exclusion criteria, concomitant medications, and the management of cabazitaxel-related toxicity.
03 April 2015	- Decreased the concentration of cabazitaxel infusion by lowering the high end of the range from 0.26 mg/mL to 0.18 mg/mL. - Added pre-steroid treatment at 24 hours and 12 hours before each cabazitaxel infusion (pre-steroid treatment was to be given at 24 hours, 12 hours and 30 minutes – 60 minutes before each cabazitaxel dosing). - Adjusted the dose (0.5 mg/kg) and the range (from 0.01 - 0.25 mg/kg to 0.05 - 0.1 mg/kg) of dexamethasone. - Capped each dose of dexamethasone at 10 mg maximum.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported