Clinical trial results:
A Phase 1/2 Study Evaluating Intermittent and Continuous OSI 906 and Weekly Paclitaxel in Patients with Recurrent Epithelial Ovarian Cancer (and Other Solid Tumors)

Summary

EudraCT number	2009-010319-34
Trial protocol	GB PL CZ IT
Global end of trial date	31 October 2013
Results information	
Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	31 July 2015

Trial information

Trial identification	
Sponsor protocol code	OSI-906-202
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00889382
WHO universal trial number (UTN)	-
Other trial identifiers	International Study Number (ISN): 7487-CL-0202

Notes:

Sponsors	
Sponsor organisation name	Astellas Pharma Global Development, Inc.
Sponsor organisation address	1 Astellas Way, Northbrook, IL, United States, 60062
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2013
Global end of trial reached?	Yes
Global end of trial date	31 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary phase 1 objective of the study was to determine both the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of intermittent and continuous linsitinib in combination with weekly paclitaxel in patients with advanced solid tumors. The primary objective of the phase 2 portion of this study was to determine progression-free survival (PFS) evaluated by the investigator of 2 different schedules of linsitinib (Arm A and Arm B) in combination with weekly paclitaxel as compared with paclitaxel alone (Arm C) in recurrent/refractory ovarian cancer patients.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH GCP Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	United Kingdom: 40
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Switzerland: 23
Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	210
EEA total number of subjects	100

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)	166
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted in the following locations: Phase 1: Switzerland, Canada, United Kingdom and United States. Phase 2: Australia, Canada, Czech Republic, Italy, Poland, Romania, Russia, Switzerland, United Kingdom, and United States. The principal investigator at each site was experienced in the therapeutic area of oncology.

Pre-assignment

Screening details:

Screening procedures included physical examination, vital signs and laboratory assessments. Patients were evaluated weekly at the study centers. Every 21 days will be considered 1 treatment period, except in phase 1, in which Treatment Period 1 was 28 days.

Period 1

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

Blinding implementation details:

This was an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1 Arm A- Intermittent OSI-906 300 mg QD with paclitaxel

Arm description:

Phase 1, Arm A – Intermittent OSI-906 300 mg quaque die (QD) (once daily) on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The starting dose of intermittent linsitinib was 300 mg daily on days 1 to 3 every 7 days. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 1 Arm A –Intermittent OSI-906 QD on Days 1 – 3, 8 – 10, and 15 – 17 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24. The starting dose of intermittent linsitinib was 300 mg daily on days 1 to 3 every 7 days. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to take the dose any time during that same day for intermittent schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all A Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP

1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 1 Arm A- Intermittent OSI-906 400 mg QD with paclitaxel

Arm description:

Phase 1, Arm A – Intermittent OSI-906 400 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 400 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 1 Arm A –Intermittent 400 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24. The intermittent linsitinib dose was 400 mg daily on days 1 to 3 every 7 days. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to take the dose any time during that same day for intermittent schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all A Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 1 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel

Arm description:

Phase 1, Arm A – Intermittent OSI-906 450 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 450 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200

mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 1 Arm A –Intermittent 450 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24. The intermittent linsitinib dose was 450 mg daily on days 1 to 3 every 7 days. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to take the dose any time during that same day for intermittent schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all A Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel

Arm description:

Phase 1, Arm A – Intermittent OSI-906 600 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 600 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 1 Arm A –Intermittent 600 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24. The intermittent linsitinib dose was 600 mg daily on days 1 to 3 every 7 days. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to take the dose any time during that same day for intermittent schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all A Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel

Arm description:

Phase 1, Arm B: Continuous OSI-906 bis in die (BID) (twice daily) from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 75 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 1, Arm B: Continuous OSI-906 BID (Days 1 – 28) (for TP 1); all other treatment period (TPs): continuous OSI-906 BID (Days 1 – 21). The starting dose of continuous linsitinib was 75 mg twice daily. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to skip the missed dose and take the next dose for continuous schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all B Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel

Arm description:

Phase 1, Arm B: Continuous OSI-906 150 mg BID from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 150 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to

the dose level to which they were enrolled. For phase 1, Arm B: Continuous OSI-906 150 mg BID (Days 1 – 28) (for TP 1); all other treatment period (TPs): continuous OSI-906 BID (Days 1 – 21). The continuous linsitinib dose was 150 mg twice daily for this arm. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to skip the missed dose and take the next dose for continuous schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. All patients were to receive paclitaxel premedication as per local practices. For phase 1, all B Arms, paclitaxel was given on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1, paclitaxel was given on Days 8, 15, and 22). On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion. Paclitaxel was administered on day 8 (not on day 1) for the first treatment period only in order to obtain single-agent pharmacokinetics for linsitinib and to assess any potential drug-drug interaction. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously, which was considered an acceptable standard based on available literature for the weekly administration of paclitaxel.

Arm title	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel

Arm description:

Phase 2, Arm A – 600 mg intermittent linsitinib once daily on days 1 to 3, 8 to 10, and 15 to 17 with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Arm type	Experimental
Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 2, Arm A – Intermittent OSI-906 QD on Days 1 – 3, 8 – 10, and 15 – 17. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to take the dose any time during that same day for intermittent schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. For phase 2, Arm A, 80 mg/m^2 paclitaxel intravenously on days 1, 8, and 15 of every 21-day treatment period. On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion.

Arm title	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel

Arm description:

Phase 2, Arm B – 150 mg twice daily continuous linsitinib from day 1 onwards with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Arm type	Experimental

Investigational medicinal product name	OSI-906
Investigational medicinal product code	ASP7487
Other name	Linsitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The Sponsor supplied OSI-906/linsitinib as tablets. Linsitinib was to be taken with food and up to 200 mL of water. Patients were instructed to take the correct number of linsitinib tablets corresponding to the dose level to which they were enrolled. For phase 2, Arm B – 150 mg twice daily continuous linsitinib from day 1 onwards. Doses were to be taken at approximately the same time each day and at regular intervals (approximately every 12 hours). If a patient missed a dose of linsitinib, the missed dose should not have been taken with the subsequent dose. The patient was allowed to skip the missed dose and take the next dose for continuous schedule.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. For phase 2, Arm B, 80 mg/m^2 paclitaxel intravenously on days 1, 8, and 15 of every 21-day treatment period. On days when both study drugs were co-administered (linsitinib and paclitaxel), the linsitinib dose was to be taken 2 hours prior to initiating the paclitaxel infusion.

Arm title	Phase 2 Arm C - 80 mg/m^2 paclitaxel

Arm description:

Phase 2, Arm C – 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP. During phase 2, patients were stratified according to the following criteria: a) number of prior chemotherapy regimens (1 vs. 2); and b) outcome of most recent platinum-containing chemotherapy regimen – refractory (Progressive disease (PD) on most recent platinum-containing chemotherapy) vs. resistant (PD within 6 months of stopping most recent platinum-containing chemotherapy).

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

Dosage and administration details:

Weekly paclitaxel was to be administered as an intravenous formulation over a 1-hour period according to institution practice. For phase 2, Arm C, 80 mg/m^2 paclitaxel intravenously on days 1, 8, and 15 of every 21-day treatment period.

Number of subjects in period 1	Phase 1 Arm A-Intermittent OSI-906 300 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 400 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 450 mg QD with paclitaxel
Started	4	3	14
Completed	0	0	0
Not completed	4	3	14
Randomized but never received study drug	-	-	-
Physician decision	-	-	-
Disease progression	3	1	10

Crossed over to continuous linsitinib 150 mg QD	-	-	-
Death	-	-	-
Medical or ethical reasons	-	1	1
Adverse event	1	-	3
Other: clinical progression related to ascites	-	-	-
Withdrew consent	-	-	-
Other: Medical or ethical reasons	-	-	-
Other: Patient had travel plans	-	-	-
Withdrawal by subject	-	1	-

Number of subjects in period 1	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel
Started	6	3	28
Completed	0	0	0
Not completed	6	3	28
Randomized but never received study drug	-	-	-
Physician decision	-	-	-
Disease progression	5	3	19
Crossed over to continuous linsitinib 150 mg QD	-	-	-
Death	-	-	-
Medical or ethical reasons	-	-	3
Adverse event	1	-	5
Other: clinical progression related to ascites	-	-	-
Withdrew consent	-	-	-
Other: Medical or ethical reasons	-	-	-
Other: Patient had travel plans	-	-	-
Withdrawal by subject	-	-	1

Number of subjects in period 1	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel	Phase 2 Arm C - 80 mg/m^2 paclitaxel
Started	51	51	50
Completed	0	0	0
Not completed	51	51	50
Randomized but never received study drug	1	2	1
Physician decision	1	3	3
Disease progression	39	32	28
Crossed over to continuous linsitinib 150 mg QD	1	5	4
Death	-	1	-

Medical or ethical reasons	-	-	-
Adverse event	5	4	8
Other: clinical progression related to ascites	-	1	-
Withdrew consent	4	3	4
Other: Medical or ethical reasons	-	-	1
Other: Patient had travel plans	-	-	1
Withdrawal by subject	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 300 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 300 mg quaque die (QD) (once daily) on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The starting dose of intermittent linsitinib was 300 mg daily on days 1 to 3 every 7 days. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 400 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 400 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 400 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 450 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 450 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 600 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 600 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 bis in die (BID) (twice daily) from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 75 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 150 mg BID from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 150 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Reporting group title	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel

Reporting group description:

Phase 2, Arm A – 600 mg intermittent linsitinib once daily on days 1 to 3, 8 to 10, and 15 to 17 with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Reporting group title	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel

Reporting group description:

Phase 2, Arm B – 150 mg twice daily continuous linsitinib from day 1 onwards with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Reporting group title	Phase 2 Arm C - 80 mg/m^2 paclitaxel

Reporting group description:

Phase 2, Arm C – 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP. During phase 2, patients were stratified according to the following criteria: a) number of prior chemotherapy regimens (1 vs. 2); and b) outcome of most recent platinum-containing chemotherapy regimen – refractory (Progressive disease (PD) on most recent platinum-containing chemotherapy) vs. resistant (PD within 6 months of stopping most recent platinum-containing chemotherapy).

Reporting group values	Phase 1 Arm A-Intermittent OSI-906 300 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 400 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 450 mg QD with paclitaxel
Number of subjects	4	3	14
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
For phase 1 the age values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 age values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: years			
arithmetic mean	62.8	61.7	55.3
standard deviation	± 7.59	± 0.58	± 9.35
Gender categorical			
For phase 1 the gender values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 gender values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: Subjects			
Female	3	2	13
Male	1	1	1

Reporting group values	Phase 1 Arm A-Intermittent OSI-906 600 mg QD with paclitaxel	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel
Number of subjects	6	3	28
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
For phase 1 the age values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 age values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: years			
arithmetic mean	58.5	60.7	56.9
standard deviation	± 8.8	± 2.08	± 9.75
Gender categorical			
For phase 1 the gender values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 gender values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: Subjects			
Female	5	3	23
Male	1	0	5

Reporting group values	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel	Phase 2 Arm C - 80 mg/m^2 paclitaxel
Number of subjects	51	51	50
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
For phase 1 the age values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 age values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: years			
arithmetic mean	57.84	57.96	56.4
standard deviation	± 10.68	± 8.407	± 9.198
Gender categorical			
For phase 1 the gender values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 gender values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: Subjects			

Female	51	51	50
Male	0	0	0

Reporting group values	Total		
Number of subjects	210		
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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
For phase 1 the age values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 age values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
For phase 1 the gender values were based on the Safety Analysis Set (SAF), the SAF consisted of all enrolled patients who received at least 1 dose of study drug. For phase 2 gender values were based on the Full Analysis Set (FAS), the FAS consisted of all randomized patients.			
Units: Subjects			
Female	201		
Male	9		

End points

End points reporting groups

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 300 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 300 mg quaque die (QD) (once daily) on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The starting dose of intermittent linsitinib was 300 mg daily on days 1 to 3 every 7 days. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 400 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 400 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 400 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 450 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 450 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 600 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 600 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 bis in die (BID) (twice daily) from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 75 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 150 mg BID from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 150 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Reporting group title	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel

Reporting group description:

Phase 2, Arm A – 600 mg intermittent linsitinib once daily on days 1 to 3, 8 to 10, and 15 to 17 with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Reporting group title	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel

Reporting group description:

Phase 2, Arm B – 150 mg twice daily continuous linsitinib from day 1 onwards with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Reporting group title	Phase 2 Arm C - 80 mg/m^2 paclitaxel

Reporting group description:

Phase 2, Arm C – 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP. During phase 2, patients were stratified according to the following criteria: a) number of prior chemotherapy regimens (1 vs. 2); and b) outcome of most recent platinum-containing chemotherapy regimen – refractory (Progressive disease (PD) on most recent platinum-containing chemotherapy) vs. resistant (PD within 6 months of stopping most recent platinum-containing chemotherapy).

Subject analysis set title	Phase 1 Arm A- Intermittent OSI-906 once daily with paclitaxel
Subject analysis set type	Full analysis

Subject analysis set description:

The MTD Determination Analysis Set (MTDSET) was defined as all patients who were considered fully evaluable for assessment of Dose-limiting toxicity (DLT) or experienced DLTs. Patients who required a dose interruption or reduction during the initial 28-day treatment period remained evaluable for MTD determination if the reason for the reduction and/or interruption represented a DLT. A standard 3+3 dose escalation scheme was used. The dose-limiting toxicities were listed for the MTD determining patients. Patients were treated in either the intermittent or continuous linsitinib (in combination with weekly paclitaxel) arm.

Subject analysis set title	Phase 1 Arm B - Continuous OSI-906 twice daily with paclitaxel
Subject analysis set type	Full analysis

Subject analysis set description:

Population MTDSET.

Primary: Phase 1: Determine the Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D)

End point title	Phase 1: Determine the Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D)[1]

End point description:

The MTD Determination Analysis Set (MTDSET) was defined as all patients who were considered fully evaluable for assessment of Dose-limiting toxicity (DLT) or experienced DLTs. Patients who required a dose interruption or reduction during the initial 28-day treatment period remained evaluable for MTD determination if the reason for the reduction and/or interruption represented a DLT. A standard 3+3 dose escalation scheme was used. The dose-limiting toxicities were listed for the MTD determining patients. Patients were treated in either the intermittent or continuous linsitinib (in combination with weekly paclitaxel) arm.

End point type	Primary

End point timeframe:

28 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: No statistical analysis provided for Maximum Tolerated Dose (MTD), not applicable.

End point values	Phase 1 Arm A- Intermittent OSI-906 once daily with paclitaxel	Phase 1 Arm B - Continuous OSI-906 twice daily with paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	9		
Units: mg				
number (not applicable)				
MTD and RP2D [N= 12, 6]	600	150		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Progression Free Survival (PFS)

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

End point description:

The primary efficacy variable for this study was PFS based on the RECIST (v1.1), which only included the disease progression assessment from the radiological review. The hazard ratio of the treatment effect along with 95% CI was calculated using Cox proportional hazard model. The study analysis population consisted of the Full Analysis Set (FAS), the FAS consisted of all randomized patients.

End point type	Primary

End point timeframe:

Up to 15 months.

Notes:

[2] - 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: This endpoint was only applicable to the arms in the phase 2 portion of the trial.

End point values	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel	Phase 2 Arm C - 80 mg/m^2 paclitaxel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	51	50	
Units: Percentage				
number (not applicable)	76.5	74.5	66	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Unstratified hazard ratio for linsitinib/paclitaxel arm vs paclitaxel alone arm. Assuming proportional hazards, a hazard ratio less than 1 indicates a reduction in hazard rate in favor of linsitinib.

Comparison groups	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel v Phase 2 Arm C - 80 mg/m^2 paclitaxel
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2678
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.303
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.813
upper limit	2.089

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Unstratified hazard ratio for linsitinib/paclitaxel arm vs paclitaxel alone arm. Assuming proportional hazards, a hazard ratio less than 1 indicates a reduction in hazard rate in favor of linsitinib.	
Comparison groups	Phase 2 Arm C - 80 mg/m^2 paclitaxel v Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4522
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.195
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.749
upper limit	1.909

Adverse events information

Timeframe for reporting adverse events:

A Treatment Emergent Adverse Event (TEAE) was defined as any adverse event (i.e., a new event or an exacerbation of a pre-existing condition) that occurred after the patient was enrolled and up to 30 days after the last study drug administration.

Adverse event reporting additional description:

An adverse event (AE) or adverse experience was defined as any untoward medical occurrence in a study patient who was administered a study drug that did not necessarily have a causal relationship with this treatment. All of the AEs with an onset date after the first dose of linsitinib for Arm C patients were considered as treatment emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel

Reporting group description:

Phase 2, Arm A – 600 mg intermittent linsitinib once daily on days 1 to 3, 8 to 10, and 15 to 17 with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day treatment period (TP).

Reporting group title	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel

Reporting group description:

Phase 2, Arm B – 150 mg twice daily continuous linsitinib from day 1 onwards with 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP.

Reporting group title	Phase 2 Arm C - 80 mg/m^2 paclitaxel

Reporting group description:

Phase 2, Arm C – 80 mg/m^2 paclitaxel on days 1, 8, and 15 of every 21-day TP. During phase 2, patients were stratified according to the following criteria: a) number of prior chemotherapy regimens (1 vs. 2); and b) outcome of most recent platinum-containing chemotherapy regimen – refractory (Progressive disease (PD) on most recent platinum-containing chemotherapy) vs. resistant (PD within 6 months of stopping most recent platinum-containing chemotherapy).

Reporting group title	Phase 2 Arm C Crossover

Reporting group description:

Twelve patients crossed over from treatment with paclitaxel alone in Arm C to be treated with single-agent linsitinib (150 mg continuous twice daily dosing). Of these 12 patients, 1 patient died before receiving treatment and a second patient was confirmed to have progressive disease and no treatment was given. Thus, 10 patients were actually treated with linsitinib in the crossover group. These patients were analyzed separately and are referred to as Arm C crossover patients.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 300 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 quaque die (QD) (once daily) on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except Treatment Period 1 (TP 1); in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The starting dose of intermittent linsitinib was 300 mg daily on days 1 to 3 every 7 days. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 400 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 400 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 400 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 450 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 450 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel

Reporting group description:

Phase 1, Arm A – Intermittent OSI-906 600 mg QD on Days 1 – 3, 8 – 10, and 15 – 17 with paclitaxel on Days 1, 8, and 15 (except TP 1; in TP 1 OSI-906 on Days 1 – 3, 8 –10, 15 – 17, and 22 – 24 with paclitaxel on Days 8, 15, and 22). The intermittent linsitinib dose was 600 mg daily on days 1 to 3 every 7 days for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 bis in die (BID) (twice daily) from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 75 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Reporting group title	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel

Reporting group description:

Phase 1, Arm B: Continuous OSI-906 150 mg BID from Day 1 onwards with paclitaxel on Days 1, 8, and 15; (except TP 1; in TP 1 OSI-906 from Day 1 with paclitaxel on Days 8, 15, and 22). The continuous linsitinib dose was 150 mg twice daily for this arm. The planned starting dose of paclitaxel was 80 mg/m^2 intravenously. Arm B, continuous OSI-906 in combination with weekly paclitaxel, was divided into 3 subset groups: Arm B1 – TP 1: continuous OSI-906 BID (Days 1 – 21); Arm B2 – TP 1: Continuous OSI-906 BID (Days 1 – 28) (additional PK sampling on Day 9 or 13 or 14 for TP 1); Arm B3 – TP 1: continuous OSI-906 BID (Days 1 – 28) (OSI-906 dosing 2 hours prior to the initiation of paclitaxel infusion in TP 1 Day 8 only) all other TPs no separation in OSI-906 and paclitaxel dosing.

Serious adverse events	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel	Phase 2 Arm C - 80 mg/m^2 paclitaxel
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 50 (36.00%)	19 / 49 (38.78%)	17 / 49 (34.69%)
number of deaths (all causes)	1	8	4
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 50 (0.00%)	3 / 49 (6.12%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Ovarian cancer recurrent			

subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Malignant pleural effusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
Arteriosclerosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Cardiovascular insufficiency			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Embolism			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
Asthenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Sudden death			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Reproductive system and breast disorders			
Vaginal fistula			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Haemoptysis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Haemoglobin decreased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Platelet count decreased			

subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Blood creatinine increased			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Stent-graft malfunction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Femoral neck fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Lung injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Pelvic fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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

Myocardial ischaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
Dystonia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Embolic cerebral infarction			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Tremor			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Convulsion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Syncope			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Coagulopathy			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Febrile neutropenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Abdominal pain			
subjects affected / exposed	1 / 50 (2.00%)	3 / 49 (6.12%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ascites			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic stenosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Constipation			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Gastrointestinal disorder			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Haematemesis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Ileus			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 50 (0.00%)	4 / 49 (8.16%)	4 / 49 (8.16%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
Nausea			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Oesophagitis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Vomiting			
subjects affected / exposed	3 / 50 (6.00%)	2 / 49 (4.08%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	2 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Proctalgia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Gastrointestinal obstruction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Hepatobiliary disorders			
Hepatic haemorrhage			

subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal and urinary disorders			
Obstructive uropathy			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Renal failure			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Renal failure acute			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Ureteric obstruction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Intervertebral disc degeneration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Central line infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Gastrointestinal infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Sepsis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Tracheobronchitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Dehydration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Hyperkalaemia			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (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
Hypocalcaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2 Arm C Crossover	Phase 1 Arm A-Intermittent OSI-906 300 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 400 mg QD with paclitaxel
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Ovarian cancer recurrent			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Malignant pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Arteriosclerosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Cardiovascular insufficiency			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Performance status decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Sudden death			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Reproductive system and breast disorders			

Vaginal fistula			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Pneumothorax			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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 arrest			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Haemoglobin decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Stent-graft malfunction			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Femoral neck fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Lung injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Pelvic fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Dystonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Embolic cerebral infarction			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Convulsion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Coagulopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Neutropenia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Leukocytosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (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
Ascites			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (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
Colonic stenosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (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
Gastrointestinal disorder			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Haematemesis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Ileus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Intestinal obstruction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Oesophagitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Small intestinal perforation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Vomiting			

subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (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
Intestinal perforation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (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
Large intestinal obstruction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (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
Proctalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (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
Gastrointestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
Obstructive uropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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 failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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 failure acute			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Ureteric obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Intervertebral disc degeneration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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

Central line infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Arthritis bacterial			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Tracheobronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Urinary tract infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Hypercalcaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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
Hypocalcaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (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 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	2 / 3 (66.67%)
number of deaths (all causes)	0	1	2

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Ovarian cancer recurrent			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Malignant pleural effusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Arteriosclerosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Cardiovascular insufficiency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Embolism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Performance status decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Sudden death			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Reproductive system and breast disorders			
Vaginal fistula			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Pleural effusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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

Pneumonitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Pneumothorax			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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 arrest			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (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
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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

Haemoglobin decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Blood creatinine increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Stent-graft malfunction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Femoral neck fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Pelvic fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Dystonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Embolic cerebral infarction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Tremor			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Convulsion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (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
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Coagulopathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Leukopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Leukocytosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Abdominal distension			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Ascites			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Colonic stenosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Gastrointestinal disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Haematemesis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Ileus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Intestinal obstruction			

subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (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
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Oesophagitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Small intestinal perforation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Intestinal perforation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Proctalgia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Gastrointestinal obstruction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Obstructive uropathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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 failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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 failure acute			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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

Groin pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Intervertebral disc degeneration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Central line infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Sepsis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Arthritis bacterial			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Tracheobronchitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
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			
Anorexia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Hypercalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Hyperglycaemia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (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 Arm B - Continuous OSI-906 150 mg BID with paclitaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 28 (53.57%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ovarian cancer recurrent			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant pleural effusion			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiovascular insufficiency			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Performance status decreased				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Reproductive system and breast disorders				
Vaginal fistula				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pleural effusion				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram T wave inversion				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin decreased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stent-graft malfunction			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung injury			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Supraventricular tachycardia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dystonia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolic cerebral infarction			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coagulopathy			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Febrile neutropenia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Colonic stenosis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorder				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				

subjects affected / exposed	2 / 28 (7.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Small intestinal perforation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal obstruction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic haemorrhage				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Obstructive uropathy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure acute				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureteric obstruction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Groin pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc degeneration				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central line infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Anorexia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 2 Arm A - 600 mg intermittent OSI-906 QD with paclitaxel	Phase 2 Arm B - 150 mg BID continuous OSI-906 with paclitaxel	Phase 2 Arm C - 80 mg/m^2 paclitaxel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 50 (98.00%)	47 / 49 (95.92%)	48 / 49 (97.96%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 50 (6.00%)	1 / 49 (2.04%)	2 / 49 (4.08%)
occurrences (all)	3	1	15
Deep vein thrombosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hyperaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 50 (22.00%)	6 / 49 (12.24%)	4 / 49 (8.16%)
occurrences (all)	23	9	5
Chills			

subjects affected / exposed	2 / 50 (4.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	2	3	3
Fatigue			
subjects affected / exposed	23 / 50 (46.00%)	26 / 49 (53.06%)	26 / 49 (53.06%)
occurrences (all)	50	56	62
Mucosal inflammation			
subjects affected / exposed	6 / 50 (12.00%)	3 / 49 (6.12%)	6 / 49 (12.24%)
occurrences (all)	7	3	10
Oedema peripheral			
subjects affected / exposed	8 / 50 (16.00%)	4 / 49 (8.16%)	10 / 49 (20.41%)
occurrences (all)	11	7	15
Pain			
subjects affected / exposed	1 / 50 (2.00%)	3 / 49 (6.12%)	0 / 49 (0.00%)
occurrences (all)	1	3	0
Pyrexia			
subjects affected / exposed	2 / 50 (4.00%)	8 / 49 (16.33%)	6 / 49 (12.24%)
occurrences (all)	2	8	9
Influenza like illness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Catheter related complication			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Thirst			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 50 (8.00%)	5 / 49 (10.20%)	12 / 49 (24.49%)
occurrences (all)	4	14	14
Dyspnoea			
subjects affected / exposed	7 / 50 (14.00%)	7 / 49 (14.29%)	6 / 49 (12.24%)
occurrences (all)	8	19	7
Epistaxis			
subjects affected / exposed	4 / 50 (8.00%)	7 / 49 (14.29%)	5 / 49 (10.20%)
occurrences (all)	5	8	6
Nasal congestion			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Oropharyngeal pain			
subjects affected / exposed	5 / 50 (10.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	5	2	3
Dysphonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 50 (10.00%)	3 / 49 (6.12%)	5 / 49 (10.20%)
occurrences (all)	5	3	7
Abnormal dreams			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Affect lability			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Confusional state			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 50 (8.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences (all)	6	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	16 / 50 (32.00%)	2 / 49 (4.08%)	1 / 49 (2.04%)
occurrences (all)	28	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood amylase increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lipase increased			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Periorbital haematoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Splinter haemorrhages			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 50 (6.00%)	1 / 49 (2.04%)	5 / 49 (10.20%)
occurrences (all)	3	1	5
Dysgeusia			

subjects affected / exposed	2 / 50 (4.00%)	5 / 49 (10.20%)	9 / 49 (18.37%)
occurrences (all)	2	5	17
Headache			
subjects affected / exposed	6 / 50 (12.00%)	8 / 49 (16.33%)	7 / 49 (14.29%)
occurrences (all)	8	8	17
Neuropathy peripheral			
subjects affected / exposed	7 / 50 (14.00%)	8 / 49 (16.33%)	17 / 49 (34.69%)
occurrences (all)	10	15	31
Paraesthesia			
subjects affected / exposed	7 / 50 (14.00%)	7 / 49 (14.29%)	4 / 49 (8.16%)
occurrences (all)	15	12	9
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 50 (12.00%)	3 / 49 (6.12%)	5 / 49 (10.20%)
occurrences (all)	8	4	12
Somnolence			
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	4	0	0
Amnesia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 50 (22.00%)	12 / 49 (24.49%)	17 / 49 (34.69%)
occurrences (all)	25	17	26
Leukopenia			
subjects affected / exposed	2 / 50 (4.00%)	3 / 49 (6.12%)	2 / 49 (4.08%)
occurrences (all)	3	5	3
Neutropenia			
subjects affected / exposed	12 / 50 (24.00%)	3 / 49 (6.12%)	4 / 49 (8.16%)
occurrences (all)	21	4	4
Bone marrow failure			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hearing impaired			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	0	2	3
Blepharospasm			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed	1 / 50 (2.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	1	5	1
Abdominal distension			
subjects affected / exposed	7 / 50 (14.00%)	5 / 49 (10.20%)	7 / 49 (14.29%)
occurrences (all)	8	5	7
Abdominal pain			
subjects affected / exposed	10 / 50 (20.00%)	11 / 49 (22.45%)	20 / 49 (40.82%)
occurrences (all)	17	12	50
Abdominal pain lower			
subjects affected / exposed	0 / 50 (0.00%)	3 / 49 (6.12%)	0 / 49 (0.00%)
occurrences (all)	0	4	0
Abdominal pain upper			
subjects affected / exposed	6 / 50 (12.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	14	2	12
Ascites			
subjects affected / exposed	3 / 50 (6.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences (all)	4	3	3
Constipation			
subjects affected / exposed	14 / 50 (28.00%)	17 / 49 (34.69%)	16 / 49 (32.65%)
occurrences (all)	23	29	26
Dyspepsia			
subjects affected / exposed	8 / 50 (16.00%)	3 / 49 (6.12%)	6 / 49 (12.24%)
occurrences (all)	11	3	6
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 50 (6.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences (all)	3	1	1
Nausea			
subjects affected / exposed	30 / 50 (60.00%)	16 / 49 (32.65%)	23 / 49 (46.94%)
occurrences (all)	60	28	41
Stomatitis			
subjects affected / exposed	7 / 50 (14.00%)	3 / 49 (6.12%)	4 / 49 (8.16%)
occurrences (all)	8	3	5
Vomiting			
subjects affected / exposed	17 / 50 (34.00%)	7 / 49 (14.29%)	16 / 49 (32.65%)
occurrences (all)	40	10	43
Diarrhoea			

subjects affected / exposed	23 / 50 (46.00%)	15 / 49 (30.61%)	13 / 49 (26.53%)
occurrences (all)	35	25	29
Haemorrhoids			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gastric haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tongue discolouration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 50 (20.00%)	15 / 49 (30.61%)	19 / 49 (38.78%)
occurrences (all)	28	19	25
Drug eruption			
subjects affected / exposed	9 / 50 (18.00%)	4 / 49 (8.16%)	5 / 49 (10.20%)
occurrences (all)	16	8	10
Dry skin			
subjects affected / exposed	4 / 50 (8.00%)	2 / 49 (4.08%)	5 / 49 (10.20%)
occurrences (all)	4	5	5
Erythema			
subjects affected / exposed	0 / 50 (0.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	0	3	7
Nail discolouration			
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	5 / 49 (10.20%)
occurrences (all)	0	3	7
Nail disorder			
subjects affected / exposed	5 / 50 (10.00%)	5 / 49 (10.20%)	11 / 49 (22.45%)
occurrences (all)	8	15	13

Onychalgia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	3 / 49 (6.12%)
occurrences (all)	0	0	4
Pruritus			
subjects affected / exposed	4 / 50 (8.00%)	4 / 49 (8.16%)	2 / 49 (4.08%)
occurrences (all)	6	10	3
Rash			
subjects affected / exposed	6 / 50 (12.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences (all)	6	6	6
Skin reaction			
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences (all)	4	0	1
Skin oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Bladder spasm			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 50 (4.00%)	6 / 49 (12.24%)	7 / 49 (14.29%)
occurrences (all)	4	8	15
Back pain			
subjects affected / exposed	2 / 50 (4.00%)	4 / 49 (8.16%)	4 / 49 (8.16%)
occurrences (all)	2	4	4
Groin pain			

subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	4	0	0
Muscle spasms			
subjects affected / exposed	3 / 50 (6.00%)	4 / 49 (8.16%)	2 / 49 (4.08%)
occurrences (all)	3	5	2
Musculoskeletal pain			
subjects affected / exposed	2 / 50 (4.00%)	0 / 49 (0.00%)	3 / 49 (6.12%)
occurrences (all)	8	0	4
Myalgia			
subjects affected / exposed	3 / 50 (6.00%)	6 / 49 (12.24%)	3 / 49 (6.12%)
occurrences (all)	5	9	14
Pain in extremity			
subjects affected / exposed	6 / 50 (12.00%)	2 / 49 (4.08%)	4 / 49 (8.16%)
occurrences (all)	6	2	6
Bone pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Nodule on extremity			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 50 (2.00%)	2 / 49 (4.08%)	3 / 49 (6.12%)
occurrences (all)	2	3	3
Nail infection			
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences (all)	1	1	3
Nasopharyngitis			
subjects affected / exposed	3 / 50 (6.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	4	3	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 50 (4.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	2	5	1
Urinary tract infection			
subjects affected / exposed	3 / 50 (6.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	3	4	2
Anal infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Application site infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Candidiasis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Cystitis escherichia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Escherichia urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Sinusitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	4 / 50 (8.00%)	12 / 49 (24.49%)	8 / 49 (16.33%)
occurrences (all)	5	20	10
Dehydration			
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	2 / 49 (4.08%)
occurrences (all)	4	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 50 (2.00%)	5 / 49 (10.20%)	3 / 49 (6.12%)
occurrences (all)	1	15	3
Hypokalaemia			
subjects affected / exposed	3 / 50 (6.00%)	2 / 49 (4.08%)	2 / 49 (4.08%)
occurrences (all)	6	2	2
Hypomagnesaemia			
subjects affected / exposed	1 / 50 (2.00%)	2 / 49 (4.08%)	4 / 49 (8.16%)
occurrences (all)	2	2	8
Hyponatraemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hyperlipasaemia			

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hyperphagia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 Arm C Crossover	Phase 1 Arm A-Intermittent OSI-906 300 mg QD with paclitaxel	Phase 1 Arm A-Intermittent OSI-906 400 mg QD with paclitaxel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	4 / 4 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	5

Chills			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	3 / 4 (75.00%)	2 / 3 (66.67%)
occurrences (all)	1	5	7
Mucosal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	2 / 10 (20.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	3
Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Catheter related complication			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Thirst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	3 / 4 (75.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Abnormal dreams			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Affect lability			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood amylase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	8
International normalised ratio increased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Excoriation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Splinter haemorrhages			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Neuropathy peripheral			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amnesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Balance disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Parosmia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	5
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone marrow failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hearing impaired			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blepharospasm			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual impairment			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	2 / 10 (20.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	6	2	1
Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 10 (20.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Ascites			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 10 (20.00%)	2 / 4 (50.00%)	2 / 3 (66.67%)
occurrences (all)	4	2	4
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 4 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	6	4
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	3 / 4 (75.00%)	2 / 3 (66.67%)
occurrences (all)	4	5	2
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	2 / 4 (50.00%)	3 / 3 (100.00%)
occurrences (all)	4	6	4
Haemorrhoids			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Proctalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Breath odour			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cheilitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastric haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Haematochezia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tongue discolouration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	0	2	3
Drug eruption			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	0	2	6
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Nail discolouration			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	1 / 10 (10.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Onychalgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin oedema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin hyperpigmentation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Bladder spasm			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary hesitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	5
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Nodule on extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nail infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Anal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Application site infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bronchitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis escherichia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 10 (10.00%)	3 / 4 (75.00%)	1 / 3 (33.33%)
occurrences (all)	1	5	1
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperlipasaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperphagia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1 Arm A- Intermittent OSI-906 450 mg QD with paclitaxel	Phase 1 Arm A- Intermittent OSI-906 600 mg QD with paclitaxel	Phase 1 Arm B - Continuous OSI-906 75 mg BID with paclitaxel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	6 / 6 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	2
Hyperaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypotension			

subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	1	1	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Chills			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	7 / 14 (50.00%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	20	10	10
Mucosal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	3	1	8
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter related complication			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Early satiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Infusion site pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Food allergy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	4	0	3
Dyspnoea			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	7	1	0
Epistaxis			
subjects affected / exposed	6 / 14 (42.86%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	9	1	3
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	3
Dysphonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	4
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Productive cough			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pulmonary congestion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Sinus congestion			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Throat irritation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0

Abnormal dreams			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Affect lability			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood amylase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urine present			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
International normalised ratio increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Weight increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Excoriation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Periorbital haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper limb fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Splinter haemorrhages			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Dysgeusia			
subjects affected / exposed	5 / 14 (35.71%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	6	1	1
Headache			
subjects affected / exposed	6 / 14 (42.86%)	0 / 6 (0.00%)	3 / 3 (100.00%)
occurrences (all)	12	0	3
Neuropathy peripheral			
subjects affected / exposed	5 / 14 (35.71%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	14	1	5
Paraesthesia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 14 (21.43%)	3 / 6 (50.00%)	0 / 3 (0.00%)
occurrences (all)	9	5	0
Somnolence			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Amnesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			

subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
Lethargy			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Memory impairment			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Parosmia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Restless legs syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinus headache			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Speech disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 14 (14.29%)	3 / 6 (50.00%)	2 / 3 (66.67%)
occurrences (all)	9	4	3
Leukopenia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0

Neutropenia			
subjects affected / exposed	4 / 14 (28.57%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	9	1	2
Bone marrow failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hearing impaired			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blepharospasm			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			

subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	3 / 14 (21.43%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Visual impairment			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	3 / 14 (21.43%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Abdominal pain			
subjects affected / exposed	4 / 14 (28.57%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	7	4	0
Abdominal pain lower			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 14 (14.29%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Ascites			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Constipation			
subjects affected / exposed	3 / 14 (21.43%)	4 / 6 (66.67%)	0 / 3 (0.00%)
occurrences (all)	5	4	0
Dyspepsia			
subjects affected / exposed	6 / 14 (42.86%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Nausea			
subjects affected / exposed	12 / 14 (85.71%)	4 / 6 (66.67%)	3 / 3 (100.00%)
occurrences (all)	20	9	10
Stomatitis			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	2	1	4
Vomiting			
subjects affected / exposed	6 / 14 (42.86%)	1 / 6 (16.67%)	3 / 3 (100.00%)
occurrences (all)	8	2	9
Diarrhoea			
subjects affected / exposed	8 / 14 (57.14%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	15	13	9
Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Breath odour			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Eructation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Gastric haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Melaena			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tongue discolouration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Umbilical hernia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 14 (35.71%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	10	6	4
Drug eruption			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	5	1	9
Dry skin			

subjects affected / exposed	4 / 14 (28.57%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	7	1	0
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nail discolouration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	4	1	1
Onychalgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	4 / 14 (28.57%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	8	1	3
Skin reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Palmar erythema			

subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	2
Rash erythematous			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bladder spasm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	5	2	2
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Pollakiuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Urinary hesitation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Urinary incontinence			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	4	1	0

Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	4	1	14
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	2 / 6 (33.33%)	2 / 3 (66.67%)
occurrences (all)	2	3	3
Groin pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	3 / 14 (21.43%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Myalgia			
subjects affected / exposed	3 / 14 (21.43%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	3	1	4
Pain in extremity			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	10
Bone pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Muscle twitching			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Nodule on extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain in jaw			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nail infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	3
Anal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Application site infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	4
Cystitis escherichia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Localised infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Paronychia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Tooth abscess			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection bacterial			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	3 / 14 (21.43%)	2 / 6 (33.33%)	2 / 3 (66.67%)
occurrences (all)	3	2	3
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypokalaemia			

subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	2 / 3 (66.67%)
occurrences (all)	2	1	3
Hypomagnesaemia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	5	2	0
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	2 / 14 (14.29%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Hyperlipasaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperphagia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	Phase 1 Arm B - Continuous OSI-906 150 mg BID with paclitaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Deep vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Hot flush			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hyperaemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	19		
Chills			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	20 / 28 (71.43%)		
occurrences (all)	63		
Mucosal inflammation			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	8		
Pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Catheter related complication			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Early satiety			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Infusion site pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Thirst			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Food allergy			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 28 (35.71%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	8		
Epistaxis			

subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	3			
Nasal congestion				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	3			
Oropharyngeal pain				
subjects affected / exposed	4 / 28 (14.29%)			
occurrences (all)	5			
Dysphonia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Dyspnoea exertional				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	4			
Haemoptysis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	2			
Nasal dryness				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	3			
Paranasal sinus hypersecretion				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Productive cough				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	2			
Pulmonary congestion				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Rhinorrhoea				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Sinus congestion				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Throat irritation				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	5		
Abnormal dreams			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Affect lability			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Confusional state			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	7		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Blood amylase increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Blood urine present			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Excoriation			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Periorbital haematoma			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Skin laceration			

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Upper limb fracture			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Splinter haemorrhages			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	4		
Dysgeusia			
subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	10		
Neuropathy peripheral			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	13		
Paraesthesia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	9		
Somnolence			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Amnesia			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Ataxia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	4		
Balance disorder			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Memory impairment			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Parosmia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Peripheral motor neuropathy			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	5		
Restless legs syndrome			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Sinus headache			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Speech disorder			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	8		
Leukopenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Bone marrow failure			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Deafness			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hearing impaired			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hypoacusis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Blepharospasm			

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Lacrimation increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	10		
Abdominal pain lower			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	9 / 28 (32.14%)		
occurrences (all)	11		

Dyspepsia				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	15 / 28 (53.57%)			
occurrences (all)	23			
Stomatitis				
subjects affected / exposed	5 / 28 (17.86%)			
occurrences (all)	7			
Vomiting				
subjects affected / exposed	9 / 28 (32.14%)			
occurrences (all)	15			
Diarrhoea				
subjects affected / exposed	16 / 28 (57.14%)			
occurrences (all)	28			
Haemorrhoids				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Proctalgia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Rectal haemorrhage				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Breath odour				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Cheilitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Dry mouth				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			

Eructation subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Gastric haemorrhage subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Gingival pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Haematochezia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Hyperchlorhydria subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Melaena subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Oesophagitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Tongue discolouration subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Umbilical hernia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Skin and subcutaneous tissue disorders Alopecia			

subjects affected / exposed	14 / 28 (50.00%)			
occurrences (all)	16			
Drug eruption				
subjects affected / exposed	5 / 28 (17.86%)			
occurrences (all)	5			
Dry skin				
subjects affected / exposed	5 / 28 (17.86%)			
occurrences (all)	6			
Erythema				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Nail discolouration				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Nail disorder				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	4			
Onychalgia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	4 / 28 (14.29%)			
occurrences (all)	5			
Skin reaction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Skin oedema				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Dermatitis contact				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Hyperhidrosis				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Ingrowing nail			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Palmar erythema			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Periorbital oedema			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Skin hyperpigmentation			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Bladder spasm			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

Urinary hesitation			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	11		
Back pain			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	6		
Groin pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	5		
Musculoskeletal pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	7		
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Muscle twitching			

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Nodule on extremity			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nail infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	6		
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

Anal infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Application site infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Candidiasis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Cystitis escherichia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Fungal infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Localised infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			

Oral herpes			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Otitis media			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Sepsis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Urinary tract infection bacterial			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	9		
Dehydration			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	9		
Hypokalaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Hypomagnesaemia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Hyponatraemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hyperlipasaemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hyperphagia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2010	Amendment 1, Version 2: The primary purpose of this amendment was to modify the pharmacokinetic sampling in Arm B2.
16 May 2011	Amendment 2, Version 3 : Thirty-seven patients were enrolled in phase 2 of the study under Amendment 2.
18 August 2011	Amendment 2.1 (United Kingdom): The primary purpose of this amendment was to include information on the incidence and severity of hypoglycemia and provide guidance for managing and reporting hypoglycemia.
07 February 2012	Amendment 3, Version 4: Eighty-eight patients were enrolled in phase 2 of the study under Amendment 3.
30 October 2012	Amendment 4, Version 5: Sixteen patients were enrolled in phase 2 of the study under Amendment 4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported