Clinical trial results:
A Multicenter, Open-Label, Phase 2 Study to Evaluate the Safety and Efficacy of NKTR-102 (PEG-Irinotecan) When Given on a Q14 Day or a Q21 Day Schedule in Patients with Metastatic or Unresectable Locally Advanced Platinum-Resistant Ovarian Cancer

Summary

EudraCT number	2008-005576-26
Trial protocol	BE GB
Global end of trial date	30 October 2012

Results information

Result version number	v1 (current)
This version publication date	05 August 2017
First version publication date	05 August 2017

Trial information

Trial identification

Sponsor protocol code	08-PIR-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00806156
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nektar Therapeutics
Sponsor organisation address	455 Mission Bay Boulevard South, San Francisco, United States, CA 94158
Public contact	Nektar Therapeutics, Nektar Therapeutics, 001 415.482.5300, StudyInquiry@nektar.com
Scientific contact	Nektar Therapeutics, Nektar Therapeutics, 001 415.482.5300, StudyInquiry@nektar.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	05 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 October 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

For the Primary Efficacy Population:
•To determine the objective response rate (ORR) with NKTR-102 given on a once every 21 days (q21d) treatment schedule in patients with platinum-resistant ovarian cancer and who have received prior pegylated liposomal doxorubicin (PLD) therapy in a platinum-resistant setting or who were otherwise unable to receive further PLD therapy.

Protection of trial subjects:

This study was carried out in compliance with the International Conference on Harmonisation harmonized Tripartite Guidelines for Good Clinical Practice 1996, the United States (US) 21 Code of Federal Regulations dealing with clinical studies (including Parts 50 and 56 concerning informed consent and IRB regulations) and the Declaration of Helsinki, concerning medical research in humans (Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects, Helsinki 1964, amended Tokyo 1975, Venice 1983, Hong Kong 1989, Somerset West, South Africa, 1996, Edinburgh 2000, Washington 2002, Tokyo 2004, and Seoul 2008). Before implementing this study, the protocol, the proposed Informed Consent Form, and other information to patients were reviewed by a properly constituted Institutional Review Board (IRB) or Independent Ethics Committee (IEC) for each study site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 43
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	United States: 83
Worldwide total number of subjects	178
EEA total number of subjects	95

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)	126
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Before any protocol-specific procedures are initiated, each patient and the Investigator were to sign and date an IRB or IEC-approved informed consent form. All patients considered for this study had to satisfy all eligibility criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	NKTR-102 q14d

Arm description:

NKTR-102 was administered as an intravenous (IV) infusion over 90 ± 10 minutes, on Day 1 of each 2-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 4 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.

Arm type	Experimental
Investigational medicinal product name	NKTR-102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

NKTR-102 was reconstituted in 5% dextrose and was administered as an IV infusion over 90 ± 10 minutes, on Day 1 of each 14-day [± 2 days] cycle at a dose of 170mg/m^2 for the first 4 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients. Body surface area was determined based on baseline height and current weight before the start of each cycle. The NKTR-102 drug product was formulated as a sterile lyophilized powder of NKTR-102 in lactate buffer at pH 3.5 supplied in 25 mL type-I amber-coloured glass vials. Specific NKTR-102 dose modifications could be made for drug-related neutropenia, thrombocytopenia, anaemia, diarrhoea, and other drug-related, non-haematological adverse events. Study drug was continued until disease progression, unacceptable toxicity, death, withdrawal by patient, Principal Investigator decision, lost to follow-up, protocol violation, or study termination by Sponsor.

Arm title	NKTR-102 q21d

Arm description:

NKTR-102 was administered as an IV infusion over 90 ± 10 minutes, on Day 1 of each 3-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 6 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.

Arm type	Experimental
Investigational medicinal product name	NKTR-102
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

NKTR-102 was reconstituted in 5% dextrose and was administered as an IV infusion over 90 ± 10 minutes, on Day 1 of each 21-day [± 2 days] cycle at a dose of 170mg/m^2 for the first 6 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients. Body surface area was determined based on baseline height and current weight before the start of each cycle. The NKTR-102

drug product was formulated as a sterile lyophilized powder of NKTR-102 in lactate buffer at pH 3.5 supplied in 25 mL type-I amber-coloured glass vials. Specific NKTR-102 dose modifications could be made for drug-related neutropenia, thrombocytopenia, anaemia, diarrhoea, and other drug-related, non-haematological adverse events. Study drug was continued until disease progression, unacceptable toxicity, death, withdrawal by patient, Principal Investigator decision, lost to follow-up, protocol violation, or study termination by Sponsor.

Number of subjects in period 1	NKTR-102 q14d	NKTR-102 q21d
Started	39	139
Completed	0	0
Not completed	39	139
Consent withdrawn by subject	1	3
Study terminated by Sponsor	2	40
Death	35	95
Other	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	NKTR-102 q14d
Reporting group description:	
NKTR-102 was administered as an intravenous (IV) infusion over 90 ± 10 minutes, on Day 1 of each 2-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 4 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.	
Reporting group title	NKTR-102 q21d
Reporting group description:	
NKTR-102 was administered as an IV infusion over 90 ± 10 minutes, on Day 1 of each 3-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 6 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.	

Reporting group values	NKTR-102 q14d	NKTR-102 q21d	Total
Number of subjects	39	139	178
Age categorical Units: Subjects			
18 to 64 years	27	99	126
65 to 84 years	12	40	52
Age continuous Units: years			
arithmetic mean	58.5	58.3	
standard deviation	± 12.14	± 11.49	-
Gender categorical Units: Subjects			
Female	39	139	178

End points reporting groups

Reporting group title	NKTR-102 q14d

Reporting group description:

NKTR-102 was administered as an intravenous (IV) infusion over 90 ± 10 minutes, on Day 1 of each 2-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 4 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.

Reporting group title	NKTR-102 q21d

Reporting group description:

NKTR-102 was administered as an IV infusion over 90 ± 10 minutes, on Day 1 of each 3-week [± 2 days] cycle at a dose of 170 mg/m^2 for the first 6 patients enrolled and at a dose of 145 mg/m^2 for the remainder of the patients.

Subject analysis set title	MITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified intent-to-treat (MITT) Population for the q14d Arm included all platinum-resistant ovarian cancer patients who were enrolled to the q14d treatment regimen. The MITT Population for the q21d Arm included all platinum-resistant ovarian cancer patients who were enrolled to the q21d treatment regimen. The MITT Population included those patients who had undergone radiographic tumor measurement evaluation at Baseline with measurable tumors, and were enrolled and received at least one dose (or partial dose) of study drug. Platinum-resistant patients had a platinum-free interval (PFI) ≤ 6 months. PFI was defined as the time to recurrence/progression from last dose of the prior platinum-based therapy.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of all patients who received at least one dose (or partial dose) of the study drug.

Subject analysis set title	Prior PLD Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the MITT Population treated in q14d and q21d treatment schedules, who subsequently progressed after receiving PLD therapy or who were otherwise unable to receive PLD therapy.

Subject analysis set title	Primary Efficacy Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the MITT Population treated in q21d treatment schedule with platinum-resistant ovarian cancer, had received prior PLD therapy in a platinum-resistant setting or who were otherwise unable to receive further PLD therapy.

Subject analysis set title	Platinum-Refractory Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the MITT Population with a PFI ≤ 6 weeks.

Primary: Objective Response Rate (ORR) by Response Evaluation Criteria in Solid Tumors (RECIST): Primary Efficacy Population

End point title	Objective Response Rate (ORR) by Response Evaluation Criteria in Solid Tumors (RECIST): Primary Efficacy Population[1][2]

End point description:

The ORR was defined as the proportion of patients with a complete response (CR) or a partial response (PR) per RECIST 1.0 based upon the best response as assessed by the Investigator. The analysis was performed for patients in the Primary Efficacy Population.

End point type	Primary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

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: Per the protocol, the planned analysis was descriptive only.

[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: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Percentage of Patients				
number (confidence interval 95%)	14.4 (8.3 to 22.7)	14.4 (8.3 to 22.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response by Gynecologic Cancer Intergroup (GCIG) Criteria: MITT Population

End point title	Best Overall Response by Gynecologic Cancer Intergroup (GCIG) Criteria: MITT Population

End point description:

Best overall response was defined as the proportion of patients with a CR or a PR as assessed per GCIG criteria. The GCIG proposed the following definition for the date of progression which used both the RECIST and cancer antigen 125 (CA-125) criteria. "A response according to CA-125 has occurred if there is ≥ 50% reduction in CA-125 levels from a pretreatment sample. The response had to be confirmed and maintained for at least 28 days. Patients can be evaluated according to CA-125 only if they had a pretreatment sample that was at least twice the upper limit of normal (ULN) and within 2 weeks prior to starting treatment." Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Percentage of Patients				
number (confidence interval 95%)	29.7 (15.9 to 47)	25 (17.9 to 33.3)	26 (19.6 to 33.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response by GCIG Criteria: Primary Efficacy Population

End point title	Best Overall Response by GCIG Criteria: Primary Efficacy Population[3]

End point description:

Best overall response was defined as the proportion of patients with a CR or a PR per assessed per GCIG criteria. The GCIG proposed the following definition for the date of progression which used both the RECIST and CA-125 criteria. "A response according to CA-125 has occurred if there is ≥ 50% reduction in CA-125 levels from a pretreatment sample. The response had to be confirmed and maintained for at least 28 days. Patients can be evaluated according to CA-125 only if they had a pretreatment sample that was at least twice the ULN and within 2 weeks prior to starting treatment." Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Percentage of Patients				
number (confidence interval 95%)	25 (17 to 34.4)	25 (17 to 34.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response by GCIG Criteria: Platinum-Refractory Population

End point title	Best Overall Response by GCIG Criteria: Platinum-Refractory Population

End point description:

Best overall response was defined as the proportion of patients with a CR or a PR per assessed per GCIG criteria. The GCIG proposed the following definition for the date of progression which used both the RECIST and CA-125 criteria. "A response according to CA-125 has occurred if there is ≥ 50% reduction in CA-125 levels from a pretreatment sample. The response had to be confirmed and maintained for at least 28 days. Patients can be evaluated according to CA-125 only if they had a pretreatment sample that was at least twice the ULN and within 2 weeks prior to starting treatment." Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Percentage of Patients				
number (confidence interval 95%)	23.1 (5 to 53.8)	17.3 (8.2 to 30.3)	18.5 (9.9 to 30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response by GCIG Criteria: Prior PLD Therapy Population

End point title	Best Overall Response by GCIG Criteria: Prior PLD Therapy Population

End point description:

Best overall response was defined as the proportion of patients with a CR or a PR per assessed per GCIG criteria. The GCIG proposed the following definition for the date of progression which used both the RECIST and CA-125 criteria. "A response according to CA-125 has occurred if there is ≥ 50% reduction in CA-125 levels from a pretreatment sample. The response had to be confirmed and maintained for at least 28 days. Patients can be evaluated according to CA-125 only if they had a pretreatment sample that was at least twice the ULN and within 2 weeks prior to starting treatment." Analysis was performed in Prior PLD Therapy Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Percentage of patients				
number (confidence interval 95%)	25 (7.3 to 52.4)	24.6 (17 to 33.5)	24.6 (17.5 to 32.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS): MITT Population

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS): MITT Population

End point description:

PFS was defined as the time from the date of the first NKTR-102 administration to the date of progressive disease (PD) or death due to any cause. Progressive disease was determined by Investigators using RECIST criteria. Patients who were alive without disease progression at the time of data-cut-off were censored at the time of the last tumor assessment that demonstrated a lack of disease progression (or on Cycle 1 Day 1 if the patient did not undergo repeated imaging while on study). Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Months				
median (confidence interval 95%)	4.1 (2.6 to 6.7)	4.4 (2.9 to 5)	4.4 (3.1 to 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of PFS: Primary Efficacy Population

End point title	Kaplan-Meier Estimate of PFS: Primary Efficacy Population[4]

End point description:

PFS was defined as the time from the date of the first NKTR-102 administration to the date of PD or death due to any cause. Progressive disease was determined by Investigators using RECIST criteria. Patients who were alive without disease progression at the time of data-cut-off were censored at the time of the last tumor assessment that demonstrated a lack of disease progression (or on Cycle 1 Day 1 if the patient did not undergo repeated imaging while on study). Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Months				
median (confidence interval 95%)	4.4 (2.9 to 5)	4.4 (2.9 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of PFS: Platinum-Refractory Population

End point title	Kaplan-Meier Estimate of PFS: Platinum-Refractory Population

End point description:

PFS was defined as the time from the date of the first NKTR-102 administration to the date of PD or death due to any cause. Progressive disease was determined by Investigators using RECIST criteria. Patients who were alive without disease progression at the time of data-cut-off were censored at the time of the last tumor assessment that demonstrated a lack of disease progression (or on Cycle 1 Day 1 if the patient did not undergo repeated imaging while on study). Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Months				
median (confidence interval 95%)	11.9 (2 to 15)	2.7 (1.7 to 4.6)	3 (2 to 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of PFS: Prior PLD Therapy Population

End point title	Kaplan-Meier Estimate of PFS: Prior PLD Therapy Population

End point description:

PFS was defined as the time from the date of the first NKTR-102 administration to the date of PD or death due to any cause. Progressive disease was determined by Investigators using RECIST criteria. Patients who were alive without disease progression at the time of data-cut-off were censored at the time of the last tumor assessment that demonstrated a lack of disease progression (or on Cycle 1 Day 1 if the patient did not undergo repeated imaging while on study). Analysis was performed in Prior PLD Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Months				
median (confidence interval 95%)	5.5 (2.2 to 11.4)	4.4 (2.9 to 5)	4.5 (3.1 to 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of Duration of Overall Response (DoR): MITT Population

End point title	Kaplan-Meier Analysis of Duration of Overall Response (DoR): MITT Population

End point description:

DoR was defined as the time from the first documented CR or PR, the date of PD (assessed by central radiological review according to RECIST), or death due to any cause, whichever came first. Patients who were alive without documented PD per RECIST were censored at the date of last tumor assessment without disease progression or start of new anti-cancer therapy for the study disease, whichever was earlier. Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

From the time measurement criteria for CR/PR (whichever was first recorded) were first met until the first date that recurrent disease or PD or death was objectively documented.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Months				
median (confidence interval 95%)	4.1 (2.8 to 8)	6.6 (3.6 to 10.9)	5.7 (4 to 10.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of DoR: Primary Efficacy Population

End point title	Kaplan-Meier Analysis of DoR: Primary Efficacy Population[5]

End point description:

DoR was defined as the time from the first documented CR or PR, the date of PD (assessed by central radiological review according to RECIST), or death due to any cause, whichever came first. Patients who were alive without documented PD per RECIST were censored at the date of last tumor assessment without disease progression or start of new anti-cancer therapy for the study disease, whichever was earlier. Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

From the time measurement criteria for CR/PR (whichever was first recorded) were first met until the first date that recurrent disease or PD or death was objectively documented.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Months				
median (confidence interval 95%)	7.4 (3.6 to 13.2)	7.4 (3.6 to 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of DoR: Platinum-Refractory Population

End point title	Kaplan-Meier Analysis of DoR: Platinum-Refractory Population

End point description:

DoR was defined as the time from the first documented CR or PR, the date of PD (assessed by central radiological review according to RECIST), or death due to any cause, whichever came first. Patients who were alive without documented PD per RECIST were censored at the date of last tumor assessment without disease progression or start of new anti-cancer therapy for the study disease, whichever was earlier. Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

From the time measurement criteria for CR/PR (whichever was first recorded) were first met until the first date that recurrent disease or PD or death was objectively documented.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Months				
median (confidence interval 95%)	10.8 (7.1 to 14.4)	7.4 (2.9 to 12.6)	7.4 (2.9 to 12.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of DoR: Prior PLD Therapy Population

End point title	Kaplan-Meier Analysis of DoR: Prior PLD Therapy Population

End point description:

DoR was defined as the time from the first documented CR or PR, the date of PD (assessed by central radiological review according to RECIST), or death due to any cause, whichever came first. Patients who were alive without documented PD per RECIST were censored at the date of last tumor assessment without disease progression or start of new anti-cancer therapy for the study disease, whichever was earlier. Analysis was performed in Prior PLD Therapy Population.

End point type	Secondary

End point timeframe:

From the time measurement criteria for CR/PR (whichever was first recorded) were first met until the first date that recurrent disease or PD or death was objectively documented.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Months				
median (confidence interval 95%)	4.2 (4.1 to 14.4)	7.4 (3.6 to 10.9)	6.6 (4 to 10.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: CA-125 Response Rate: MITT Population

End point title	CA-125 Response Rate: MITT Population

End point description:

CA-125 response was determined by having achieved a ≥50% reduction in serum levels of CA-125 from a pre-treatment level of at least twice the ULN within 2 weeks of starting treatment according to the GCIG criteria. The CA-125 response rate was calculated as the number of patients meeting the endpoint definition divided by the total number of eligible patients per the GCIG criteria for CA-125 in the analysis population. Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

Every 4 weeks from Cycle 1, Day 1 until end-of-treatment (EOT) visit.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	109	141	
Units: Percentage of Patients				
number (confidence interval 95%)	43.8 (26.4 to 62.3)	34.9 (26 to 44.6)	36.9 (28.9 to 45.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: CA-125 Response Rate: Primary Efficacy Population

End point title	CA-125 Response Rate: Primary Efficacy Population[6]

End point description:

CA-125 response was determined by having achieved a ≥50% reduction in serum levels of CA-125 from a pre-treatment level of at least twice the ULN within 2 weeks of starting treatment according to the GCIG criteria. The CA-125 response rate was calculated as the number of patients meeting the endpoint definition divided by the total number of eligible patients per the GCIG criteria for CA-125 in the analysis population. Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

Every 4 weeks from Cycle 1, Day 1 until EOT visit.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	88	88		
Units: Percentage of Patients				
number (confidence interval 95%)	33 (23.3 to 43.8)	33 (23.3 to 43.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: CA-125 Response Rate: Platinum-Refractory Population

End point title	CA-125 Response Rate: Platinum-Refractory Population

End point description:

CA-125 response was determined by having achieved a ≥50% reduction in serum levels of CA-125 from a pre-treatment level of at least twice the ULN within 2 weeks of starting treatment according to the

GCIG criteria. The CA-125 response rate was calculated as the number of patients meeting the endpoint definition divided by the total number of eligible patients per the GCIG criteria for CA-125 in the analysis population. Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

Every 4 weeks from Cycle 1, Day 1 until EOT visit.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	11	40	51	
Units: Percentage of Patients				
number (confidence interval 95%)	36.4 (10.9 to 69.2)	20 (9.1 to 35.6)	23.5 (12.8 to 37.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: CA-125 Response Rate: Prior PLD Therapy Population

End point title	CA-125 Response Rate: Prior PLD Therapy Population

End point description:

CA-125 response was determined by having achieved a ≥50% reduction in serum levels of CA-125 from a pre-treatment level of at least twice the ULN within 2 weeks of starting treatment according to the GCIG criteria. The CA-125 response rate was calculated as the number of patients meeting the endpoint definition divided by the total number of eligible patients per the GCIG criteria for CA-125 in the analysis population. Analysis was performed in Prior PLD Therapy Population.

End point type	Secondary

End point timeframe:

Every 4 weeks from Cycle 1, Day 1 until EOT visit.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	95	110	
Units: Percentage of Patients				
number (confidence interval 95%)	40 (16.3 to 67.7)	33.7 (24.3 to 44.1)	34.5 (25.7 to 44.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate: MITT Population

End point title	Clinical Benefit Rate: MITT Population

End point description:

Clinical benefit rate was calculated as the number of patients with confirmed CR, PR, or SD (where the duration of SD should be ≥ 3 months) by RECIST divided by the total number of measurable patients in the population. Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Percentage of Patients				
number (confidence interval 95%)	56.8 (39.5 to 72.9)	50.8 (41.9 to 59.6)	52.1 (44.3 to 59.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate: Primary Efficacy Population

End point title	Clinical Benefit Rate: Primary Efficacy Population[7]

End point description:

Clinical benefit rate was calculated as the number of patients with confirmed CR, PR, or SD (where the duration of SD should be ≥ 3 months) by RECIST divided by the total number of measurable patients in the population. Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Percentage of Patients				
number (confidence interval 95%)	51 (41 to 60.9)	51 (41 to 60.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate: Platinum-Refractory Population

End point title	Clinical Benefit Rate: Platinum-Refractory Population

End point description:

Clinical benefit rate was calculated as the number of patients with confirmed CR, PR, or SD (where the duration of SD should be ≥ 3 months) by RECIST divided by the total number of measurable patients in the population. Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Percentage of Patients				
number (confidence interval 95%)	61.5 (31.6 to 86.1)	38.5 (25.3 to 53)	43.1 (30.8 to 56)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate: Prior PLD Therapy Population

End point title	Clinical Benefit Rate: Prior PLD Therapy Population

End point description:

Clinical benefit rate was calculated as the number of patients with confirmed CR, PR, or SD (where the duration of SD should be ≥ 3 months) by RECIST divided by the total number of measurable patients in the population. Analysis was performed in Prior PLD Therapy Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Percentage of Patients				
number (confidence interval 95%)	56.3 (29.9 to 80.2)	50.9 (41.3 to 60.4)	51.5 (42.6 to 60.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of Overall Survival (OS): MITT Population

End point title	Kaplan-Meier Analysis of Overall Survival (OS): MITT Population

End point description:

Duration of OS was defined as the time from the date of randomization to the date of death due to any cause. Patients were followed until their date of death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure. Patients who were lost-to-follow-up or were not known to have died were censored at last date they were shown to be alive. Patients who did not have any follow-up since the date of randomization were censored at the date of randomization. Analysis was performed in MITT Population.

End point type	Secondary

End point timeframe:

From randomization to death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Months				
median (confidence interval 95%)	11.1 (8.8 to 16.7)	10.2 (8.2 to 12.2)	10.6 (9.4 to 12.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of OS: Primary Efficacy Population

End point title	Kaplan-Meier Analysis of OS: Primary Efficacy Population[8]

End point description:

Duration of OS was defined as the time from the date of randomization to the date of death due to any cause. Patients were followed until their date of death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure. Patients who were lost-to-follow-up or were not known to have died were censored at last date they were shown to be alive. Patients who did not have any follow-up since the date of randomization were censored at the date of randomization. Analysis was performed in Primary Efficacy Population.

End point type	Secondary

End point timeframe:

From randomization to death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The primary efficacy population only included subjects treated in the NKTR-102 q21d treatment arm.

End point values	NKTR-102 q21d	Primary Efficacy Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: Months				
median (confidence interval 95%)	10.9 (8.2 to 13.1)	10.9 (8.2 to 13.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of OS: Platinum-Refractory Population

End point title	Kaplan-Meier Analysis of OS: Platinum-Refractory Population

End point description:

Duration of OS was defined as the time from the date of randomization to the date of death due to any cause. Patients were followed until their date of death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure. Patients who were lost-to-follow-up or were not known to have died were censored at last date they were shown to be alive. Patients who did not have any follow-up since the date of randomization were censored at the date of randomization. Analysis was performed in Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

From randomization to death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Months				
median (confidence interval 95%)	11.1 (6.1 to 21.6)	8 (5 to 12.2)	9.4 (5.8 to 12.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Analysis of OS: Prior PLD Therapy Population

End point title	Kaplan-Meier Analysis of OS: Prior PLD Therapy Population

End point description:

Duration of OS was defined as the time from the date of randomization to the date of death due to any cause. Patients were followed until their date of death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure. Patients who were lost-to-follow-up or were not known to have died were censored at last date they were shown to be alive. Patients who did not have any follow-up since the date of randomization were censored at the date of randomization. Analysis was performed in Prior PLD Therapy Population.

End point type	Secondary

End point timeframe:

From randomization to death, loss to follow-up, withdrawal of consent for further follow-up for survival, or final database closure.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Months				
median (confidence interval 95%)	12.2 (8.8 to 16.7)	11 (8.9 to 13.1)	11 (9.5 to 12.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by RECIST: MITT Population

End point title	ORR by RECIST: MITT Population

End point description:

The ORR was defined as the proportion of patients with a CR or a PR per RECIST 1.0 based upon the best response as assessed by the Investigator assessment. The analysis was performed for patients in the MITT Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	MITT Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	37	132	169	
Units: Percentage of patients				
number (confidence interval 95%)	21.6 (9.8 to 38.2)	15.2 (9.5 to 22.4)	16.6 (11.3 to 23)	

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by RECIST: Prior PLD Population

End point title	ORR by RECIST: Prior PLD Population

End point description:

The ORR was defined as the proportion of patients with a CR or a PR per RECIST 1.0 based upon the best response as assessed by the Investigator assessment. The analysis was performed for patients in the PLD Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Prior PLD Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	114	130	
Units: Percentage of patients				
number (confidence interval 95%)	18.8 (4 to 45.6)	14.9 (8.9 to 22.8)	15.4 (9.7 to 22.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by RECIST: Platinum-Refractory Population

End point title	ORR by RECIST: Platinum-Refractory Population

End point description:

The ORR was defined as the proportion of patients with a CR or a PR per RECIST 1.0 based upon the best response as assessed by the Investigator assessment. The analysis was performed for patients in the Platinum-Refractory Population.

End point type	Secondary

End point timeframe:

Every 6 weeks (± 5 days) from Cycle 1, Day 1 until documented disease progression, start of new therapy for cancer, death, or end of study.

End point values	NKTR-102 q14d	NKTR-102 q21d	Platinum-Refractory Population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	52	65	
Units: Percentage of patients				
number (confidence interval 95%)	15.4 (1.9 to 45.4)	15.4 (6.9 to 28.1)	15.4 (7.6 to 26.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events and serious adverse events were reported from the time the patient received the first dose of study drug through the End-of-Treatment Visit (30 ± 3 days after the last dose of study drug).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	NKTR-102 q14d
Reporting group description: -	
Reporting group title	NKTR-102 q21d

Reporting group description: -

Serious adverse events	NKTR-102 q14d	NKTR-102 q21d	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 38 (60.53%)	78 / 139 (56.12%)	
number of deaths (all causes)	35	95	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Disease progression			
subjects affected / exposed	2 / 38 (5.26%)	11 / 139 (7.91%)	
occurrences causally related to treatment / all	0 / 2	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 8	
Fatigue			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oedema peripheral			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 38 (2.63%)	4 / 139 (2.88%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 38 (2.63%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 38 (7.89%)	4 / 139 (2.88%)	
occurrences causally related to treatment / all	1 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Blood potassium decreased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Body temperature increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Overdose			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholinergic syndrome			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complex partial seizures			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Speech disorder			

subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 38 (0.00%)	3 / 139 (2.16%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 38 (0.00%)	3 / 139 (2.16%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 38 (5.26%)	7 / 139 (5.04%)	
occurrences causally related to treatment / all	0 / 2	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 38 (2.63%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic obstruction			

subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	9 / 38 (23.68%)	21 / 139 (15.11%)	
occurrences causally related to treatment / all	10 / 10	24 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	3 / 38 (7.89%)	7 / 139 (5.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal perforation			
subjects affected / exposed	0 / 38 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Large intestinal obstruction			
subjects affected / exposed	1 / 38 (2.63%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 38 (2.63%)	7 / 139 (5.04%)	
occurrences causally related to treatment / all	0 / 1	7 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 38 (2.63%)	11 / 139 (7.91%)	
occurrences causally related to treatment / all	0 / 1	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	3 / 38 (7.89%)	9 / 139 (6.47%)	
occurrences causally related to treatment / all	3 / 3	8 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 38 (5.26%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Renal impairment			

subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle twitching			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridial infection			
subjects affected / exposed	0 / 38 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal oesophagitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Herpes oesophagitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 38 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 38 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Staphylococcal sepsis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 38 (2.63%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	7 / 38 (18.42%)	13 / 139 (9.35%)	
occurrences causally related to treatment / all	6 / 7	9 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	NKTR-102 q14d	NKTR-102 q21d	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 38 (100.00%)	139 / 139 (100.00%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 38 (2.63%)	9 / 139 (6.47%)	
occurrences (all)	3	13	

Hypotension			
subjects affected / exposed	3 / 38 (7.89%)	6 / 139 (4.32%)	
occurrences (all)	4	6	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 38 (7.89%)	12 / 139 (8.63%)	
occurrences (all)	5	16	
Chills			
subjects affected / exposed	2 / 38 (5.26%)	7 / 139 (5.04%)	
occurrences (all)	2	11	
Fatigue			
subjects affected / exposed	20 / 38 (52.63%)	81 / 139 (58.27%)	
occurrences (all)	38	198	
Oedema peripheral			
subjects affected / exposed	7 / 38 (18.42%)	15 / 139 (10.79%)	
occurrences (all)	10	20	
Pyrexia			
subjects affected / exposed	11 / 38 (28.95%)	23 / 139 (16.55%)	
occurrences (all)	15	33	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 38 (18.42%)	13 / 139 (9.35%)	
occurrences (all)	8	14	
Dyspnoea			
subjects affected / exposed	6 / 38 (15.79%)	28 / 139 (20.14%)	
occurrences (all)	7	39	
Oropharyngeal pain			
subjects affected / exposed	3 / 38 (7.89%)	6 / 139 (4.32%)	
occurrences (all)	3	7	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 38 (18.42%)	12 / 139 (8.63%)	
occurrences (all)	8	12	
Depression			
subjects affected / exposed	3 / 38 (7.89%)	11 / 139 (7.91%)	
occurrences (all)	3	13	

Insomnia			
subjects affected / exposed	7 / 38 (18.42%)	15 / 139 (10.79%)	
occurrences (all)	8	20	
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 38 (7.89%)	10 / 139 (7.19%)	
occurrences (all)	3	14	
Haemoglobin decreased			
subjects affected / exposed	1 / 38 (2.63%)	8 / 139 (5.76%)	
occurrences (all)	1	16	
Weight decreased			
subjects affected / exposed	18 / 38 (47.37%)	42 / 139 (30.22%)	
occurrences (all)	31	51	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 38 (5.26%)	7 / 139 (5.04%)	
occurrences (all)	3	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 38 (28.95%)	25 / 139 (17.99%)	
occurrences (all)	17	36	
Dysgeusia			
subjects affected / exposed	8 / 38 (21.05%)	17 / 139 (12.23%)	
occurrences (all)	8	24	
Headache			
subjects affected / exposed	6 / 38 (15.79%)	23 / 139 (16.55%)	
occurrences (all)	13	42	
Lethargy			
subjects affected / exposed	2 / 38 (5.26%)	8 / 139 (5.76%)	
occurrences (all)	6	13	
Neuropathy peripheral			
subjects affected / exposed	4 / 38 (10.53%)	6 / 139 (4.32%)	
occurrences (all)	4	8	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 38 (26.32%)	38 / 139 (27.34%)	
occurrences (all)	19	65	

Leukopenia			
subjects affected / exposed	3 / 38 (7.89%)	13 / 139 (9.35%)	
occurrences (all)	3	43	
Neutropenia			
subjects affected / exposed	9 / 38 (23.68%)	27 / 139 (19.42%)	
occurrences (all)	22	74	
Thrombocytopenia			
subjects affected / exposed	1 / 38 (2.63%)	8 / 139 (5.76%)	
occurrences (all)	2	14	
Eye disorders			
Vision blurred			
subjects affected / exposed	9 / 38 (23.68%)	26 / 139 (18.71%)	
occurrences (all)	14	41	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	7 / 38 (18.42%)	17 / 139 (12.23%)	
occurrences (all)	8	19	
Abdominal pain			
subjects affected / exposed	16 / 38 (42.11%)	74 / 139 (53.24%)	
occurrences (all)	21	128	
Abdominal pain lower			
subjects affected / exposed	0 / 38 (0.00%)	10 / 139 (7.19%)	
occurrences (all)	0	11	
Abdominal pain upper			
subjects affected / exposed	3 / 38 (7.89%)	15 / 139 (10.79%)	
occurrences (all)	3	22	
Ascites			
subjects affected / exposed	3 / 38 (7.89%)	8 / 139 (5.76%)	
occurrences (all)	3	12	
Constipation			
subjects affected / exposed	9 / 38 (23.68%)	51 / 139 (36.69%)	
occurrences (all)	12	87	
Diarrhoea			
subjects affected / exposed	34 / 38 (89.47%)	103 / 139 (74.10%)	
occurrences (all)	230	376	
Dry mouth			

subjects affected / exposed	4 / 38 (10.53%)	5 / 139 (3.60%)	
occurrences (all)	4	6	
Dyspepsia			
subjects affected / exposed	8 / 38 (21.05%)	17 / 139 (12.23%)	
occurrences (all)	14	30	
Flatulence			
subjects affected / exposed	8 / 38 (21.05%)	16 / 139 (11.51%)	
occurrences (all)	10	19	
Nausea			
subjects affected / exposed	27 / 38 (71.05%)	107 / 139 (76.98%)	
occurrences (all)	70	250	
Stomatitis			
subjects affected / exposed	3 / 38 (7.89%)	17 / 139 (12.23%)	
occurrences (all)	8	20	
Vomiting			
subjects affected / exposed	23 / 38 (60.53%)	76 / 139 (54.68%)	
occurrences (all)	54	176	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	12 / 38 (31.58%)	29 / 139 (20.86%)	
occurrences (all)	16	35	
Dry skin			
subjects affected / exposed	3 / 38 (7.89%)	11 / 139 (7.91%)	
occurrences (all)	4	12	
Rash			
subjects affected / exposed	7 / 38 (18.42%)	17 / 139 (12.23%)	
occurrences (all)	9	23	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 38 (13.16%)	8 / 139 (5.76%)	
occurrences (all)	7	11	
Back pain			
subjects affected / exposed	4 / 38 (10.53%)	15 / 139 (10.79%)	
occurrences (all)	6	16	
Muscle spasms			

subjects affected / exposed	1 / 38 (2.63%)	16 / 139 (11.51%)	
occurrences (all)	1	25	
Muscular weakness			
subjects affected / exposed	1 / 38 (2.63%)	10 / 139 (7.19%)	
occurrences (all)	1	16	
Myalgia			
subjects affected / exposed	4 / 38 (10.53%)	8 / 139 (5.76%)	
occurrences (all)	5	15	
Pain in extremity			
subjects affected / exposed	3 / 38 (7.89%)	11 / 139 (7.91%)	
occurrences (all)	3	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 38 (13.16%)	6 / 139 (4.32%)	
occurrences (all)	5	7	
Upper respiratory tract infection			
subjects affected / exposed	3 / 38 (7.89%)	7 / 139 (5.04%)	
occurrences (all)	5	8	
Urinary tract infection			
subjects affected / exposed	6 / 38 (15.79%)	11 / 139 (7.91%)	
occurrences (all)	7	22	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	20 / 38 (52.63%)	69 / 139 (49.64%)	
occurrences (all)	35	135	
Dehydration			
subjects affected / exposed	11 / 38 (28.95%)	22 / 139 (15.83%)	
occurrences (all)	20	23	
Hypocalcaemia			
subjects affected / exposed	2 / 38 (5.26%)	7 / 139 (5.04%)	
occurrences (all)	5	10	
Hypokalaemia			
subjects affected / exposed	18 / 38 (47.37%)	28 / 139 (20.14%)	
occurrences (all)	24	61	
Hypomagnesaemia			

subjects affected / exposed	4 / 38 (10.53%)	8 / 139 (5.76%)	
occurrences (all)	4	16	
Hyponatraemia			
subjects affected / exposed	6 / 38 (15.79%)	15 / 139 (10.79%)	
occurrences (all)	6	28	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2009	1. Lowered the starting dose of NKTR-102 to 145 mg/m^2 from 170 mg/m^2. 2. Eligibility criteria changed to clarify that patients were to have metastatic or "unresectable" locally advanced platinum-resistant ovarian cancer and met eligibility criteria previously used in the Sponsor's Phase 1 study with NKTR-102 (Study 06-IN-IR001). 3. Non-treatment day study visits were removed based upon safety data obtained in Protocol 06-IN-IR001 and based upon the recommended monitoring for patients receiving Camptosar®. 4. Removed PK sampling throughout the protocol. No PK samples were collected during the study, including prior to this amendment. 5. Period of birth control changed to at least 8 months after the last dose of study drug per request from Health Canada.
30 October 2009	1. Changed the study design to include enrollment of a sub-population of patients with platinum-refractory ovarian cancer. Study enrollment was to occur in 2 parts: Part 1 would enroll patients with platinum-resistant ovarian cancer in 2 arms and 2 stages as originally intended; after Part 1 enrollment was complete, Part 2 would enroll 21 patients with platinum-refractory ovarian cancer on a q14d treatment schedule at a dose level of 145 mg/m^2. These patients with platinum-refractory ovarian cancer must have had progression by radiographic assessment on first or second line treatment with platinum-based therapy within 3 weeks of the last platinum treatment. Progression could not be determined for the platinum-refractory population by only CA-125 assessments. 2. The AE reporting and follow-up requirements were revised to require the collection and reporting of new SUSARs that are experienced by patients in the follow-up period. In addition, it also provided clarification on data entry regarding outcome of unrelated AEs that were ongoing at the time of EoT visit. 3. Clarified the language on the screening tests for hematology, chemistry, and coagulation such that screening laboratories would be performed within 28 days of the first dose of NKTR-102. 4. Increased the pretreatment interval for clinical laboratory tests from 1 day to 3 days. 5. Updated the language concerning antidiarrheal therapy. 6. Updated the pH of the formulation of NKTR-102 and the storage duration of reconstituted NKTR-102. 7. The infusion time for NKTR-102 included a window of plus or minus ten minutes. 8. Added language defining adequate forms of birth control. 9. Deleted requirement for reporting AEs using synonyms in NCI-CTCAE.
03 March 2010	1. The dosing schedule for patients in the enrollment expansion part of the study changed from q14d to q21d. 2. The eligibility criteria for defining the platinum-refractory patient population enrolled into the expansion part of the study was modified to allow a longer interval from last platinum based treatment to progression (i.e., increased from 21 days to 30 days) and removed the requirement for a minimum number of 2 cycles of platinum-based therapy prior to documented progression. 3. Clarified that only patients enrolled during the randomized part of the study (initial 2 stages of the study) could have been eligible if they had non-measurable disease and a serum CA-125 level that was at least twice the ULN within 4 weeks prior to starting study drug treatment. Patients enrolled in the expansion part of the study must have had measurable disease by radiographic assessment.

22 June 2010	1. Updated the study design and primary efficacy objective by clarifying that this is a two-stage study with two treatment arms (Arm A at 145 mg/m^2 q14d; Arm B at 145 mg/m^2 q21d); and that Arm B would enroll an additional 50 platinum-resistant ovarian cancer patients (120 patients total; 35 in Treatment Arm A and 85 in Treatment Arm B). 2. Clarified the secondary endpoints as best overall response as determined by GCIG criteria, CA-125 response rate as determined by having achieved a ≥ 50% reduction in serum CA-125 levels according to GCIG criteria, PFS by RECIST (version 1.0), and OS. 3. Clarified the eligibility criteria to include platinum-resistant patient population by removing the specifications provided for Part 2 of the study. 4. Added patients having received prior PLD therapy to the inclusion criteria. 5. Updated the justifications used to determine the sample size for Stages 1 and 2 of the study, as well as the justification used to determine the additional 50 patients who will be enrolled into Arm B of the study. 6. Clarified the primary efficacy endpoint as ORR determined by RECIST (version 1.0). 7. Added the requirement that radiographic imaging will be assessed by central independent radiologist. 8. Added a new section Evaluation of Response by RECIST (version 1.0) and corresponding table. 9. Added analysis for clinical benefit rate. 10. Added analysis for PFS relative to PFI. 11. Provided additional guidance on anti-diarrheal therapy 12. Added antiemetic therapy guidance. 13. Prospectively identified sub-populations (MITT Population, Primary Efficacy Population, Platinum-Refractory Population, and Prior PLD Therapy Population) for efficacy analyses. 14. Redefined "platinum refractory" as having a PFI ≤6 weeks.
25 March 2011	1. Updated the study design and primary efficacy objective by clarifying that Arm B of the two treatment arm, two-stage study (Arm A at 145 mg/m^2 q14d; Arm B at 145 mg/m^2 q21d) would enroll approximately 110 additional platinum-resistant ovarian cancer patients who have received prior PLD therapy in a platinum-resistant setting or who are otherwise unable to receive further PLD therapy on the q21d dosing schedule. 2. Clarified inclusion criterion #6 for patients enrolled in the study. 3. Clarified text for dose modification and dose delay scenarios. 4. Updated inclusion criterion #5 to indicate platinum-resistant ovarian cancer for this study is defined by RECIST within 6 months of last dose of most recent platinum drug. 5. Updated exclusion criterion #2 to clarify that minor surgery does not include simple ascites drains. 6. Updated the secondary objectives and endpoints to include DoR. 7. Updated the secondary endpoints by removing PFS relative to PFI. 8. Updated the justifications used to determine the sample size for Stages 1 and 2 of the study, as well as the justification used to determine the additional 110 patients who will be enrolled into Arm B. 9. Removed the 12 month of therapy measured from Cycle 1, Day 1 restriction for stopping a patient from receiving further treatment on the study. 10. Clarified the language for progression follow-up after the EOT Visit. 11. Clarified the text for radiographic scans that may be collected after the EOT Visit. 12. Updated the antidiarrheal therapy text to indicate that prophylactic antidiarrheal medications should not be used in the treatment of diarrhea AEs. 13. Provided the primary modalities for measuring response for the study. 14. Updated exploratory analyses to also include one additional possible analysis. 15. Updated Sponsor address. and the address, main fax number, and backup fax number for the Sponsor's Pharmacovigilance Designee. 16. Updated the date of the US Camptosar® Package Insert.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported