Clinical trial results:
Randomized crossover trial to assess the effects and quality of life in patients with locally advanced or metastatic pancreatic cancer treated with gemcitabine in combination with nab-paclitaxel: QOLINPAC

Summary

EudraCT number	2013-004101-75
Trial protocol	BE
Global end of trial date	29 April 2019

Results information

Result version number	v1 (current)
This version publication date	08 August 2019
First version publication date	08 August 2019
Summary attachment (see zip file)	Consort diagram (01 Qolinpac CONSORT diagram.pdf) QOL analysis methodology (02 Qolinpac QOL analysis methodology.pdf) Deaths on treatment (03 Qolinpac deaths on treatment and within 30 days from last dose.pdf) Protocol deviations (04 Qolinpac protocol deviations.pdf) Selected references (05 Qolinpac selected references.pdf) Publications (06 Qolinpac publications.pdf) Abbreviations (07 Qolinpac abbreviations.pdf)

Trial information

Trial identification

Sponsor protocol code	S56122-ML10190

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02106884
WHO universal trial number (UTN)	-
Other trial identifiers	Celgene internal number: AX-CL-PANC-PI-003568

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Prof. Dr. Eric Van Cutsem, UZ Leuven, Digestive oncology, 0032 16344225, eric.vancutsem@uzleuven.be
Scientific contact	Prof. Dr. Eric Van Cutsem, UZ Leuven, Digestive oncology, 0032 16344225, eric.vancutsem@uzleuven.be

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	29 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2019
Global end of trial reached?	Yes
Global end of trial date	29 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare quality of life scores and times to definitive deterioration of the quality of life (QOL) scores in patients receiving nab-paclitaxel (n-P) + gemcitabine (G) versus gemcitabine (G) in monotherapy using the EORTC QLQ-C30 questionnaire.

Protection of trial subjects:

Ethics review and approval, informed consent, prophylactic medication prior to infusions (to prevent chemotherapy known adverse events as per current practice and protocol recommendations), supportive care and routine monitoring.

Background therapy:

/

Evidence for comparator:

/

Actual start date of recruitment	09 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 146
Worldwide total number of subjects	146
EEA total number of subjects	146

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	76
From 65 to 84 years	70
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred fourty-six patients were included. First patient enrolled: 08-May-2014. Last patient enrolled: 25-Nov-2015. End of trial notification was dated 15-May-2018 (last patient last visit) and submitted to EC and CA 10-Jul-2018. Last follow-up (FU) data collected 05-Feb-2019. The cut off date for final data was on 29-Apr-2019.

Pre-assignment

Screening details:

The study target population was represented by patients with metastatic or unresectable locally advanced pancreatic adenocarcinoma, histologically or cytologically confirmed, eligible for treatment with gemcitabine and nab-paclitaxel in a first line setting. Patients were screened as per inclusion and exclusion criteria per protocol.

Period 1

Period 1 title	Full study duration: baseline to FU (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - nab-paclitaxel and gemcitabine

Arm description:

Patients were randomised to receive a combination regimen of nab-paclitaxel and gemcitabine.

Arm type	Experimental
Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Per protocol dose was 125 mg/m2.
Schedule: Infusions repeated for three weeks followed by a week of rest (4 week cycles). Nab-paclitaxel infusions were planned every 7 days on the same day of the week; deviations more than 2 days were not allowed.

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

Dosage and administration details:

Per protocol dose: 1000 mg/m2.
Schedule: For patients in Arm A, gemcitabine was given the same day with and following nab-paclitaxel, i.e. once weekly for 3 weeks followed by a week of rest then repeat (4 week cycles). Gemcitabine infusions were planned every 7 days on the same day of the week; deviations more than 2 days were not allowed.

Arm title	Arm B - gemcitabine monotherapy

Arm description:

Patients randomised to receive gemcitabine monotherapy.

Arm type	Standard of care - no comparator

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

Dosage and administration details:

Per protocol dose: 1000 mg/m2.
Schedule: For patients in Arm B, gemcitabine was given in an initial sequence of seven weeks followed by a week of rest (first cycle is 8 weeks) then every week for three weeks followed by a week of rest (cycle 2 and subsequent cycles are of 4 weeks). Gemcitabine infusions were planned every 7 days on the same day of the week; deviations more than 2 days were not allowed. Patients in Arm B progressing on gemcitabine monotherapy and eligible to receive nab-paclitaxel and gemcitabine were allowed to switch to the combination.

Number of subjects in period 1	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy
Started	72	74
Completed	72	73
Not completed	0	1
Change of diagnosis/exclusion criterion	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A - nab-paclitaxel and gemcitabine
Reporting group description:	
Patients were randomised to receive a combination regimen of nab-paclitaxel and gemcitabine.	
Reporting group title	Arm B - gemcitabine monotherapy
Reporting group description:	
Patients randomised to receive gemcitabine monotherapy.	

Reporting group values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Total
Number of subjects	72	74	146
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	37	76
From 65-84 years	33	37	70
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	31	32	63
Male	41	42	83
ECOG performance status			
WHO EGOG performance status (PS) scale 0 Able to carry out all normal activity without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out light work 2 Ambulatory and capable of all self-care but unable to carry out any work; up and about more than 50% of waking hours. 3 Capable of only limited self-care; confined to bed or chair more than 50% of waking hours 4 Completely disabled; cannot carry on any self-care; totally confined to bed or chair			
Units: Subjects			
PS = 0	27	23	50
PS = 1	42	49	91
PS = 2	3	2	5
Site of pancreatic tumour Units: Subjects			
Head	16	19	35
Body	37	34	71
Tail	19	21	40
Locally advanced / metastatic Units: Subjects			
Locally advanced	10	11	21
Metastatic	62	63	125

Adjuvant treatment prior to inclusion Units: Subjects			
Yes	5	6	11
No	67	68	135

Subject analysis sets

Subject analysis set title	Intent to treat set (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who consented to participate in the study and fulfilled all inclusion/exclusion criteria. One patient initially treated for pancreatic adenocarcinoma was excluded from the ITT set due to a subsequent change in diagnosis (neuroendocrine tumour).

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

Subject analysis set description:

All patients treated on trial (at least one dose of treatment).

Reporting group values	Intent to treat set (ITT)	Safety set	
Number of subjects	145	146	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	76	76	
From 65-84 years	69	70	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	63	63	
Male	82	83	
ECOG performance status			
WHO EGOG performance status (PS) scale 0 Able to carry out all normal activity without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out light work 2 Ambulatory and capable of all self-care but unable to carry out any work; up and about more than 50% of waking hours. 3 Capable of only limited self-care; confined to bed or chair more than 50% of waking hours 4 Completely disabled; cannot carry on any self-care; totally confined to bed or chair			
Units: Subjects			
PS = 0	50	50	
PS = 1	90	91	
PS = 2	5	5	
Site of pancreatic tumour Units: Subjects			
Head	34	35	
Body	71	71	
Tail	40	40	

Locally advanced / metastatic Units: Subjects			
Locally advanced	20	21	
Metastatic	125	125	
Adjuvant treatment prior to inclusion Units: Subjects			
Yes	11	11	
No	134	135	

End points

End points reporting groups

Reporting group title	Arm A - nab-paclitaxel and gemcitabine
Reporting group description:	
Patients were randomised to receive a combination regimen of nab-paclitaxel and gemcitabine.	
Reporting group title	Arm B - gemcitabine monotherapy
Reporting group description:	
Patients randomised to receive gemcitabine monotherapy.	
Subject analysis set title	Intent to treat set (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who consented to participate in the study and fulfilled all inclusion/exclusion criteria. One patient initially treated for pancreatic adenocarcinoma was excluded from the ITT set due to a subsequent change in diagnosis (neuroendocrine tumour).	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients treated on trial (at least one dose of treatment).	

Primary: Deterioration-free survival rate of the QOL global health status at 3, 6 and 12 months

End point title	Deterioration-free survival rate of the QOL global health status at 3, 6 and 12 months
End point description:	
1474 QOL questionnaires were completed (714 in arm A; 761 in arm B) The QOL global health status (GHS) is a functional parameter derived from the EORTC QLQ - C30 questionnaire, based on questions 29 "How would you rate your overall health during the past week?" and 30 "How would you rate your overall quality of life during the past week?". The deterioration free survival rate at 3 months is defined as the Kaplan-Meier estimate of the probability of being alive and free of deterioration of the QOL score at 3 months. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last FU.	
End point type	Primary
End point timeframe:	
From date of randomisation to 3, 6 and 12 months respectively	

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Rate at 3 months	89	73	81	
Rate at 6 months	74	59	66	
Rate at 12 months	40	35	38	

Attachments (see zip file)	GHS - TUDD/TUDD10_GH.jpg

Statistical analyses

Statistical analysis title	Difference in GHS deterioration-free rates 3 mo

Statistical analysis description:

Comparison of the deterioration-free survival rates based on definitive deterioration or death at 3, 6, 9, 12 months after randomisation. The comparisons are based on Z-tests after log-log transformations of the survival estimates.

Deterioration-free survival rates at 3 months were respectively: Arm A (n-P+G) 88.89%, 95%CI [79.0-94.3] and Arm B (G monotherapy) 79.74%, 95%CI [60.7-81.3] with p=0.0166. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0166 [2]
Method	Z-test

Notes:

[1] - The difference in the deterioration-free rate of the GHS at 3 months between the two arms was statistically significant.
[2] - A stratification per centre was performed. 95% confidence intervals were based on a non-parametric bootstrap procedure. The difference was still significant with p<0.05.

Primary: QOL global health status deterioration-free median survival

End point title	QOL global health status deterioration-free median survival

End point description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score or death. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last follow-up.

End point type	Primary

End point timeframe:

From date of randomisation to end of follow up (max 3 years after database lock when applicable).

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Months				
median (confidence interval 95%)	10.04 (7.16 to 12.02)	8.02 (5.49 to 11.37)	8.74 (6.67 to 10.84)	

Statistical analyses

Statistical analysis title	Deterioration-free survival time Kaplan-Meier

Statistical analysis description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score (as defined above) or death. Median times to definitive deterioration or death with 95%CI are presented for the GHS QOL score per arm. A logrank comparison between arms was performed and the p-value is provided below. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.378 [4]
Method	Logrank

Notes:

[3] - Kaplan-Meier.

[4] - The difference between arms of the median times to definitive deterioration of the GHS was not statistically significant.

Secondary: Deterioration-free survival rate of the QOL functional scales at 3, 6 and 12 months

End point title	Deterioration-free survival rate of the QOL functional scales at 3, 6 and 12 months

End point description:

The QOL functional scales are derived from the EORTC QLQ - C30: Physical functioning (PF2)Q 1-5, Role functioning (RF2) Q6&7, Emotional functioning (EF) Q21-24, Cognitive functioning (CF) Q20&25, Social functioning (SF) Q26&27. The deterioration free survival rate at 3 months is defined as the Kaplan-Meier estimate of the probability of being alive and free of deterioration of the QOL score at 3 months. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last follow-up.

End point type	Secondary

End point timeframe:

From date of randomisation to 3, 6 and 12 months respectively

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Physical functioning 3 months	76	67	72	
Physical functioning 6 months	65	57	61	
Physical functioning 12 months	32	31	31	
Role functioning 3 months	81	68	74	
Role functioning 6 months	67	53	60	
Role functioning 12 months	36	32	34	
Emotional functioning 3 months	93	79	86	
Emotional functioning 6 months	79	68	74	
Emotional functioning 12 months	40	43	42	
Cognitive functioning 3 months	89	78	83	
Cognitive functioning 6 months	75	66	70	

Cognitive functioning 12 months	40	45	42	
Social functioning 3 months	86	75	81	
Social functioning 6 months	69	64	67	
Social functioning 12 months	36	42	39	

Statistical analyses

Statistical analysis title	Difference in QOL deterioration-free rates at 3 mo

Statistical analysis description:

Comparison of the deterioration-free survival rates of the QOL functional scales based on definitive deterioration or death at 3, 6, 9, 12 months after randomisation. The comparisons are based on Z-tests after log-log transformations of the survival estimates.

Deterioration-free survival rates at 3 months difference between arms was significant for the Emotional functioning scale: Arm A (n-P+G) 93.1%, 95%CI [84.1-97.0] and Arm B (G monotherapy) 79.3%, 95%CI [68.1-87.0] with p=0.0238.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.0238 [6]
Method	z-test

Notes:

[5] - The difference in the deterioration-free rate at 3 months between the two arms was statistically significant for Emotional functioning. Additional data available upon request.
[6] - Significant for Emotional functioning.

Secondary: QOL functional scales deterioration-free median survival

End point title	QOL functional scales deterioration-free median survival

End point description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score or death. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last follow-up.

End point type	Secondary

End point timeframe:

From date of randomisation to end of follow up (max 3 years after database lock when applicable).

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Months				
median (confidence interval 95%)				
Physical functioning	7.85 (6.51 to 10.38)	6.64 (4.17 to 9.33)	7.82 (6.31 to 9.07)	

Role functioning	7.97 (6.51 to 10.58)	6.51 (4.40 to 10.18)	7.82 (6.11 to 9.00)	
Emotional functioning	10.04 (8.25 to 12.02)	11.04 (8.02 to 12.48)	10.38 (8.74 to 11.96)	
Cognitive functioning	8.87 (7.16 to 12.35)	11.37 (6.64 to 12.55)	9.92 (7.89 to 12.12)	
Social functioning	9.05 (6.90 to 11.27)	9.20 (6.11 to 12.48)	9.13 (7.59 to 11.37)	

Statistical analyses

Statistical analysis title	Deterioration-free survival time Kaplan-Meier

Statistical analysis description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score (as defined above) or death. Median times to definitive deterioration or death with 95%CI are presented for the functional QOL scales per arm. A logrank comparison between arms was performed for each scale. None of the comparisons was statistically significant. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.8408 [8]
Method	Logrank

Notes:

[7] - Kaplan-Meier.

[8] - p-value of the inter-arm comparison of the median deterioration-free survival times for Physical functioning is provided. None of the comparisons of the Functional scales were statistically significant. Additional data is available upon request.

Secondary: Deterioration-free survival rate of the QOL symptom scales at 3, 6 and 12 months

End point title	Deterioration-free survival rate of the QOL symptom scales at 3, 6 and 12 months

End point description:

The QOL symptom scales are derived from the EORTC QLQ - C30: Fatigue (FA) Q 10&12&18, Nausea and vomiting (NV) Q14&15, Pain (PA) Q9&19, Dyspnoea(DY) Q8, Insomnia (SL) Q11, Appetite loss (AP) Q13, Constipation (CO) Q16, Diarrhoea (DI) Q17, Financial difficulties (FI) Q28. The deterioration free survival rate at 3 months is defined as the Kaplan-Meier estimate of the probability of being alive and free of deterioration of the QOL score at 3 months. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last follow-up.

End point type	Secondary

End point timeframe:

From date of randomisation to 3, 6 and 12 months respectively

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Fatigue 3 months	92	79	85	
Fatigue 6 months	76	70	73	
Fatigue 12 months	47	45	46	
Nausea and vomiting 3 months	88	75	81	
Nausea and vomiting 6 months	75	63	69	
Nausea and vomiting 12 months	44	45	44	
Pain 3 months	85	71	78	
Pain 6 months	76	64	70	
Pain 12 months	39	40	40	
Dyspnoea 3 months	89	75	82	
Dyspnoea 6 months	74	67	70	
Dyspnoea 12 months	43	47	45	
Insomnia 3 months	75	74	74	
Insomnia 6 months	60	61	61	
Insomnia 12 months	38	39	38	
Appetite loss 3 months	82	70	76	
Appetite loss 6 months	64	56	60	
Appetite loss 12 months	39	35	37	
Constipation 3 months	82	74	78	
Constipation 6 months	68	63	65	
Constipation 12 months	33	38	35	
Diarrhoea 3 months	88	77	82	
Diarrhoea 6 months	72	66	69	
Diarrhoea 12 months	38	32	40	
Financial difficulties 3 months	92	79	85	
Financial difficulties 6 months	78	71	74	
Financial difficulties 12 months	43	47	45	

Statistical analyses

Statistical analysis title	Difference in QOL deterioration-free rates at 3 mo

Statistical analysis description:

Comparison of the deterioration-free survival rates of the QOL symptom scales based on definitive deterioration or death at 3, 6, 9, 12 months after randomisation. The comparisons are based on Z-tests after log-log transformations of the survival estimates.

Deterioration-free survival rates at 3 months differences between arms were significant for Fatigue p=0.0433, Dyspnoea p=0.0381 and Financial difficulties p=0.0433. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0433 [9]
Method	z-test

Notes:

[9] - p-value provided for Fatigue. Additional data available upon request.

Secondary: QOL symptom scales deterioration-free median survival

End point title	QOL symptom scales deterioration-free median survival

End point description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score or death. The definitive deterioration of the QOL score is a decrease of at least 10 points (minimal clinical important difference) as compared to the baseline score, with no further improvement of more than 10 points as compared to the score qualifying the deterioration or with no data after the deterioration was observed. Death was also considered as an event if the patient did not experience deterioration before death. Patients without event were censored at the time of last follow-up.

End point type	Secondary

End point timeframe:

From date of randomisation to end of follow up (max 3 years after database lock when applicable).

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Months				
median (confidence interval 95%)				
Fatigue	10.60 (8.25 to 14.55)	11.04 (8.44 to 13.17)	10.87 (8.97 to 12.71)	
Nausea and vomiting	10.48 (8.97 to 14.55)	10.87 (6.01 to 13.21)	10.58 (8.64 to 12.35)	
Pain	9.05 (6.97 to 11.27)	9.72 (6.44 to 13.17)	9.20 (7.82 to 11.37)	
Dyspnoea	10.27 (7.59 to 12.88)	11.43 (6.51 to 13.86)	10.58 (8.25 to 12.48)	
Insomnia	7.82 (5.55 to 10.61)	8.97 (5.62 to 12.29)	8.74 (6.28 to 10.61)	
Appetite loss	8.44 (6.28 to 11.27)	8.44 (4.63 to 11.37)	8.44 (6.18 to 10.58)	
Constipation	8.43 (6.51 to 10.38)	9.17 (6.11 to 11.73)	8.97 (6.90 to 10.58)	
Diarrhoea	8.99 (7.66 to 11.04)	9.20 (6.51 to 13.17)	9.10 (7.85 to 11.04)	
Financial difficulties	10.27 (7.66 to 12.35)	11.43 (8.71 to 13.44)	10.61 (8.71 to 12.35)	

Statistical analyses

Statistical analysis title	Deterioration-free survival time Kaplan-Meier

Statistical analysis description:

The deterioration-free survival is defined as the Kaplan-Meier estimate of median survival time to definitive deterioration of the QOL score (as defined above) or death. Median times to definitive deterioration or death with 95%CI are presented for the QOL symptom scales per arm. A logrank comparison between arms was performed for each scale. None of the comparisons was statistically significant. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.5448 [11]
Method	Logrank

Notes:

[10] - Kaplan-Meier survival analysis.

[11] - p-value of the inter-arm comparison of the median deterioration-free survival times for Fatigue is provided. None of the comparisons of the Symptom scales were statistically significant. Additional data is available upon request.

Secondary: Exposure to treatment

End point title	Exposure to treatment

End point description:

Total cumulative dose exposure is measured by dose intensity (total dose given/total dose planned*100) per drug.
The "planned dose of nab-paclitaxel" refers, as per protocol, to a weekly administration of 125 mg/m² nab-paclitaxel for 3 weeks followed by a week of rest in 4-week cycles (Arm A only). The "planned dose of gemcitabine" refers to a weekly administration of 1000 mg/m2 gemcitabine following the same day nab-paclitaxel dose in Arm A (4-week cycles) and standard in Arm B (7 infusions + 1 week of rest for cycle 1 and 4-week cycles afterwards). Total doses are the sums of all theoretical "planned" and given doses, respectively.

End point type	Secondary

End point timeframe:

From date of first infusion to date of last infusion. For patients in arm B who switched to the combination of n-P + G in second line dose exposure to n-P is given for this subset.

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Safety set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	74	146[12]	
Units: Percentage				
Nab-paclitaxel	73	74	74	
Gemcitabine	75	70	72	

Notes:

[12] - All patients received at least one dose of treatment (Safety set).

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response

End point title	Overall response

End point description:

Tumour response was assessed locally based on radiological assessments (CT/MRI) of target and non-target lesions and considering the occurrence of new lesions, as per RECIST criteria. Tumour response was defined at each evaluation as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD). Best response during treatment was selected for each patient. Overall response (OR) is defined as the best tumor response on treatment for each patient. Responders were considered CR + PR. Some patients were not evaluable for response (no scans available). Overall response rates (ORR) were calculated based on the ITT set.

End point type	Secondary

End point timeframe:

Duration of treatment

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Counts of participants				
CR + PR	31	16	47	
SD or PD	39	53	92	
Not evaluable	2	4	6	

Statistical analyses

Statistical analysis title	Overall response counts and rates

Statistical analysis description:

Descriptive. Rates of overall response (CR and PR) with 95%CI were calculated per arm: Arm A: ORR 44% 95%CI [32-56]; Arm B: ORR 23% 95%CI [13-33]. Percentages are based on evaluable patients only. A comparison between arms was performed (t-test) and the difference in response rates was statistically significant (p=0.008).

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 0.008 [14]
Method	t-test, 2-sided

Notes:

[13] - T-test double sided.

[14] - Difference between the 2 arms was statistically significant.

Secondary: Duration of response (in responders)

End point title	Duration of response (in responders)

End point description:

Duration of response was calculated from the date of first documented response to the date of progression (including SD after PR) or date of start of new treatment in not progressed, when available. In 2 patients with CR, periods of PR are included. For those not documented as progressed before death, an unknown duration was kept and considered missing data.

End point type	Secondary

End point timeframe:

Treatment

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29[15]	15[16]	44	
Units: Months				
median (full range (min-max))	6.3 (1.92 to 35)	7.4 (1.50 to 20)	6.83 (1.50 to 35)	

Notes:

[15] - 2 of 31 responders had an unknown duration of response thus not considered in this analysis

[16] - 1 of 16 responders had an unknown duration of response thus not considered in this analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control

End point title	Disease control

End point description:

Tumour response was assessed locally based on radiological assessments (CT/MRI) of target and non-target lesions and considering the occurrence of new lesions, as per RECIST criteria. Tumour response was defined at each evaluation as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD). Best response during treatment was selected for each patient. Overall response is defined as the best tumor response on treatment for each patient. Disease control is defined as a best response on treatment of either CR, PR or SD (CR + PR + SD). Some patients were not evaluable for response (no scans available). Overall response rates were calculated based on the ITT set.

End point type	Secondary

End point timeframe:

Duration of treatment

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Counts of participants				
CR + PR + SD	58	60	118	
PD	12	9	21	
Not evaluable	2	4	6	

Statistical analyses

Statistical analysis title	Disease control counts and rates

Statistical analysis description:

Descriptive. Rates of disease control (CR, PR and SD) with 95%CI were calculated per arm: Arm A: DC rate 83% 95%CI [74-92]; Arm B: OR rate 87% 95%CI [79-95]. Percentages are based on evaluable

patients only. A comparison between arms was performed (t-test) and the difference in response rates was statistically significant (p=0.503).

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.503 [18]
Method	t-test, 2-sided

Notes:

[17] - T-test double sided

[18] - Not statistically significant

Secondary: Progression rates at 1 year

End point title	Progression rates at 1 year

End point description:

Rate of progression of disease occuring within 1 year from date of randomisation are listed per arm. Details are provided in attached documents.

End point type	Secondary

End point timeframe:

1 year from date of randomisation

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Progressed at 1 year	71	79	75	
Not progressed at 1 year	29	21	25	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

Progression free survival time was considered from start of treatment until the first observation of disease progression or death from any cause, whichever occurred first. All patients (ITT).

End point type	Secondary

End point timeframe:

Treatment + follow-up

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Months				
median (confidence interval 95%)	7.01 (5.45 to 8.05)	5.06 (3.52 to 7.00)	5.85 (5.06 to 7.13)	

Statistical analyses

Statistical analysis title	Progression free survival median time Kaplan-Meier

Statistical analysis description:

The median progression free survival is defined as the Kaplan-Meier estimate of median time from randomisation to first documented progression, date of last follow-up for non progressed patients or death. Median times with 95%CI are presented per arm. A logrank comparison between arms was performed and the P value is provided below. Additional data is available upon request.

Comparison groups	Arm B - gemcitabine monotherapy v Arm A - nab-paclitaxel and gemcitabine
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.0295 [20]
Method	Logrank

Notes:

[19] - Kaplan-Meier

[20] - The difference between arms of the progression free survival time was statistically significant.

Secondary: Death rates at 30 days from last treatment

End point title	Death rates at 30 days from last treatment

End point description:

Deaths of all causes occuring between the signature of consent and the date of last infusion + 30 days for each patient are listed per arm. Only one of these fatalities was deemed possibly related to the investigational drug. Details are provided in attached documents.

End point type	Secondary

End point timeframe:

From signature of informed consent to last infusion + 30 days for each patient

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Deceased at 30 days from last treatment	7	15	11	
Alive at 30 days from last treatment	93	85	89	

Statistical analyses

No statistical analyses for this end point

Secondary: Death rates at 1 year

End point title	Death rates at 1 year

End point description:

Rate of deaths of all causes occuring within 1 year from date of randomisation are listed per arm. Details are provided in attached documents.

End point type	Secondary

End point timeframe:

1 year from the date of randomisation

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Percentage				
Deceased at 1 year	51	51	51	
Alive at 1 year	49	49	49	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was considered from start of treatment to death. All patients (ITT)

End point type	Secondary

End point timeframe:

Treatment + follow-up

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Intent to treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	73	145	
Units: Months				
median (confidence interval 95%)	10.94 (8.97 to 15.18)	11.73 (8.74 to 13.44)	11.43 (9.13 to 13.21)	

Statistical analyses

Statistical analysis title	Overall survival median time Kaplan-Meier

Statistical analysis description:

The median overall survival is defined as the Kaplan-Meier estimate of median time from randomisation to death or last follow-up. Median times to death with 95%CI are presented per arm. A logrank comparison between arms was performed and the P value is provided below. Additional data is available upon request.

Comparison groups	Arm A - nab-paclitaxel and gemcitabine v Arm B - gemcitabine monotherapy
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.7005 [22]
Method	Logrank

Notes:

[21] - Kaplan-Meier

[22] - The difference between arms of the median survival time was not statistically significant.

Secondary: Laboratory safety assessment

End point title	Laboratory safety assessment

End point description:

Severe laboratory abnormalities (hematology and biochemistry grade 3 and higher). Worst grade per patient. All patients treated (Safety set).

End point type	Secondary

End point timeframe:

From signature of informed consent to end of treatment visit plus 30 days.

End point values	Arm A - nab-paclitaxel and gemcitabine	Arm B - gemcitabine monotherapy	Safety set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	72	74[23]	146	
Units: Counts of participants				
Hemoglobin decreased	10	8	18	
Neutrophils decreased	31	31	62	
White blood cell count decreased	22	11	33	
Platelet count decreased	12	11	23	
Hyperglycemia	6	10	16	
Serum creatinine increased	0	2	2	
Bilirubin increased	3	8	11	
ALT increased	13	8	21	
AST increased	7	8	15	
ALP increased	9	11	20	
Albumin decreased	4	4	8	
Magnesium decreased	4	9	13	
Sodium decreased	8	13	21	
Potassium decreased	8	6	14	
Potassium increased	1	0	1	
Calcium decreased	3	2	5	

Notes:
[23] - Safety set - all patients.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAE) and adverse events (AE) occurring from the signature of informed consent to the end of treatment visit plus 30 days.

Adverse event reporting additional description:

All SAEs occurring between the signature of informed consent and the end of treatment visit + 30 days are listed.
Severe adverse events (grade 3-5, worst grade per patient) are listed in the non-serious AE table, SAEs are included.
A summary of the severe laboratory abnormalities is provided in section "End points".

Assessment type	Systematic

Dictionary used

Dictionary name	NCI -CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Arm A - nab-paclitaxel and gemcitabine

Reporting group description:

Patients were randomised to receive a combination regimen of nab-paclitaxel and gemcitabine

Reporting group title	ARM B - gemcitabine monotherapy

Reporting group description:

Patients randomised to receive gemcitabine in monotherapy. Some patients within this Arm switched to the combination regimen and received nab-paclitaxel with gemcitabine after the first progression on gemcitabine monotherapy. Safety set. All patients included.

Reporting group title	Total (Safety set)

Reporting group description:

Safety set. All patients included. ??? 16 deaths on trt due to all causes within 30 days from last trt -----
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Reporting group title	Subset nab-paclitaxel + gemcitabine in 2nd line

Reporting group description:

A separate additional analysis is performed for the population subset that received the combination of nab-paclitaxel and gemcitabine in second line, after the initial progression on gemcitabine monotherapy (cross-over group).

Serious adverse events	Arm A - nab-paclitaxel and gemcitabine	ARM B - gemcitabine monotherapy	Total (Safety set)
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 72 (69.44%)	48 / 74 (64.86%)	98 / 146 (67.12%)
number of deaths (all causes)	5	11	16
number of deaths resulting from adverse events	2	3	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Thromboembolic event			
subjects affected / exposed	3 / 72 (4.17%)	4 / 74 (5.41%)	7 / 146 (4.79%)
occurrences causally related to treatment / all	1 / 6	0 / 3	1 / 9
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 3
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	3 / 72 (4.17%)	5 / 74 (6.76%)	8 / 146 (5.48%)
occurrences causally related to treatment / all	2 / 3	3 / 5	5 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	9 / 72 (12.50%)	9 / 74 (12.16%)	18 / 146 (12.33%)
occurrences causally related to treatment / all	7 / 10	3 / 10	10 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flu like symptoms			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	3 / 72 (4.17%)	1 / 74 (1.35%)	4 / 146 (2.74%)
occurrences causally related to treatment / all	3 / 3	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Alteration of general condition			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Drug misuse			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalized edema			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemoptysis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary edema			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Confusion			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischemia cerebrovascular			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			

subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasovagal reaction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 72 (2.78%)	3 / 74 (4.05%)	5 / 146 (3.42%)
occurrences causally related to treatment / all	0 / 2	2 / 3	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemolytic Uremic Syndrome			
subjects affected / exposed	3 / 72 (4.17%)	2 / 74 (2.70%)	5 / 146 (3.42%)
occurrences causally related to treatment / all	3 / 3	2 / 2	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 72 (1.39%)	4 / 74 (5.41%)	5 / 146 (3.42%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ascites			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic perforation			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhea			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal and galbladder obstruction on stent			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal obstruction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric hemorrhage			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastro-enteritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sigmoiditis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic duct stenosis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	3 / 72 (4.17%)	1 / 74 (1.35%)	4 / 146 (2.74%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomach pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 72 (2.78%)	3 / 74 (4.05%)	5 / 146 (3.42%)
occurrences causally related to treatment / all	0 / 2	2 / 3	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 72 (1.39%)	3 / 74 (4.05%)	4 / 146 (2.74%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Galbladder obstruction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			

subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 72 (0.00%)	3 / 74 (4.05%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	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	3 / 72 (4.17%)	0 / 74 (0.00%)	3 / 146 (2.05%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	3 / 72 (4.17%)	3 / 74 (4.05%)	6 / 146 (4.11%)
occurrences causally related to treatment / all	2 / 3	0 / 3	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder infection			

subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	7 / 72 (9.72%)	2 / 74 (2.70%)	9 / 146 (6.16%)
occurrences causally related to treatment / all	3 / 9	1 / 2	4 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious syndrome with mastoiditis/synovitis/positive hemocultures			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic thromboflebitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Urinary tract infection			

subjects affected / exposed	4 / 72 (5.56%)	0 / 74 (0.00%)	4 / 146 (2.74%)
occurrences causally related to treatment / all	2 / 4	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	2 / 72 (2.78%)	3 / 74 (4.05%)	5 / 146 (3.42%)
occurrences causally related to treatment / all	2 / 3	0 / 4	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major denutrition			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Subset nab-paclitaxel + gemcitabine in 2nd line		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	2 / 37 (5.41%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Fever				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Flu like symptoms				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alteration of general condition				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug misuse				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalized edema				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemoptysis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary edema			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusion			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Platelet count decreased			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fracture			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischemia cerebrovascular			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vasovagal reaction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			

subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemolytic Uremic Syndrome				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombotic thrombocytopenic purpura				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colonic perforation				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Constipation			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal and galbladder obstruction on stent			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal obstruction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric hemorrhage			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstruction gastric			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastro-enteritis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sigmoiditis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic duct stenosis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomach pain			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Galbladder obstruction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholestasis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			

Hyperthyroidism				
subjects affected / exposed	0 / 37 (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	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary tract infection				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bladder infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Lung infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious syndrome with mastoiditis/synovitis/positive hemocultures				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic thromboflebitis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 37 (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 / 37 (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	2 / 37 (5.41%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Major denutrition				

subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A - nab-paclitaxel and gemcitabine	ARM B - gemcitabine monotherapy	Total (Safety set)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 72 (100.00%)	74 / 74 (100.00%)	146 / 146 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Hematoma			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	8 / 72 (11.11%)	7 / 74 (9.46%)	15 / 146 (10.27%)
occurrences (all)	12	11	23
Thromboembolic event			
subjects affected / exposed	5 / 72 (6.94%)	6 / 74 (8.11%)	11 / 146 (7.53%)
occurrences (all)	6	8	14
Hypotension			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences (all)	2	1	3
Fatigue			

subjects affected / exposed	16 / 72 (22.22%)	21 / 74 (28.38%)	37 / 146 (25.34%)
occurrences (all)	26	38	64
Fever			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Multi-organ failure			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
General status alteration			
subjects affected / exposed	1 / 72 (1.39%)	3 / 74 (4.05%)	4 / 146 (2.74%)
occurrences (all)	1	3	4
Pain			
subjects affected / exposed	1 / 72 (1.39%)	5 / 74 (6.76%)	6 / 146 (4.11%)
occurrences (all)	2	5	7
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Dyspnea			
subjects affected / exposed	6 / 72 (8.33%)	4 / 74 (5.41%)	10 / 146 (6.85%)
occurrences (all)	9	5	14
Epistaxis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Hypoxia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
COPD			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Pleural effusion			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Pumonary edema			

subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	2	2
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	2	2
Anxiety			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Investigations			
Weight loss			
subjects affected / exposed	2 / 72 (2.78%)	2 / 74 (2.70%)	4 / 146 (2.74%)
occurrences (all)	2	2	4
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Myocardial infarction			
subjects affected / exposed	0 / 72 (0.00%)	3 / 74 (4.05%)	3 / 146 (2.05%)
occurrences (all)	0	3	3
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Hemiparesis			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Peripheral motor neuropathy			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences (all)	3	0	3
Peripheral sensory neuropathy			
subjects affected / exposed	5 / 72 (6.94%)	2 / 74 (2.70%)	7 / 146 (4.79%)
occurrences (all)	6	3	9
Somnolence			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	2 / 72 (2.78%)	3 / 74 (4.05%)	5 / 146 (3.42%)
occurrences (all)	2	3	5
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	7 / 72 (9.72%)	11 / 74 (14.86%)	18 / 146 (12.33%)
occurrences (all)	9	18	27
Febrile neutropenia			
subjects affected / exposed	3 / 72 (4.17%)	0 / 74 (0.00%)	3 / 146 (2.05%)
occurrences (all)	4	0	4
Hemolytic uremic syndrome			
subjects affected / exposed	3 / 72 (4.17%)	3 / 74 (4.05%)	6 / 146 (4.11%)
occurrences (all)	3	3	6
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 72 (4.17%)	8 / 74 (10.81%)	11 / 146 (7.53%)
occurrences (all)	5	9	14
Ascites			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	2	2
Colitis			

subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Colonic obstruction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	2	2
Constipation			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	2	2
Diarrhea			
subjects affected / exposed	5 / 72 (6.94%)	2 / 74 (2.70%)	7 / 146 (4.79%)
occurrences (all)	5	2	7
Gastric ulcer			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Gastroparesis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Gastrointestinal pain			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Ileus			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Mucositis oral			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences (all)	2	0	2
Nausea			
subjects affected / exposed	5 / 72 (6.94%)	6 / 74 (8.11%)	11 / 146 (7.53%)
occurrences (all)	5	6	11
Obstruction gastric			
subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences (all)	2	1	3
Diverticulitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Intrapancreatic obstruction			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Hematemesis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Hernia inguinalis with obstruction			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Pancreatitis			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	3 / 146 (2.05%)
occurrences (all)	1	2	3
Small intestinal obstruction			
subjects affected / exposed	2 / 72 (2.78%)	2 / 74 (2.70%)	4 / 146 (2.74%)
occurrences (all)	2	3	5
Stomach pain			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	6 / 72 (8.33%)	4 / 74 (5.41%)	10 / 146 (6.85%)
occurrences (all)	6	4	10
Colonic perforation			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	2 / 72 (2.78%)	6 / 74 (8.11%)	8 / 146 (5.48%)
occurrences (all)	2	6	8
Cholecystitis			
subjects affected / exposed	1 / 72 (1.39%)	4 / 74 (5.41%)	5 / 146 (3.42%)
occurrences (all)	1	6	7
Gallbladder obstruction			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2

Hepatic failure			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	1	1	2
Cholestasis			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	3	3
Dilated bile ducts			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Jaundice			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	2 / 146 (1.37%)
occurrences (all)	2	0	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 72 (0.00%)	3 / 74 (4.05%)	3 / 146 (2.05%)
occurrences (all)	0	3	3
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	3 / 146 (2.05%)
occurrences (all)	1	2	3
Bone pain			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	2	0	2
Pain in extremity			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Infections and infestations			
Abdominal infection			

subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences (all)	2	1	3
Appendicitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	2	2
Biliary tract infection			
subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	3 / 146 (2.05%)
occurrences (all)	2	1	3
Bladder infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Bronchial infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Catheter related infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Gallbladder infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	2	0	2
Hepatic infection			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 146 (1.37%)
occurrences (all)	2	2	4
Lung infection			
subjects affected / exposed	6 / 72 (8.33%)	3 / 74 (4.05%)	9 / 146 (6.16%)
occurrences (all)	7	3	10
Infection without neutropenia NOS			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Paronychia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Pleural infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 146 (0.68%)
occurrences (all)	1	0	1
Sepsis			

subjects affected / exposed	2 / 72 (2.78%)	2 / 74 (2.70%)	4 / 146 (2.74%)
occurrences (all)	2	2	4
Tooth infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 146 (0.68%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	4 / 72 (5.56%)	0 / 74 (0.00%)	4 / 146 (2.74%)
occurrences (all)	4	0	4
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	7 / 72 (9.72%)	14 / 74 (18.92%)	21 / 146 (14.38%)
occurrences (all)	8	18	26
Dehydration			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	2 / 146 (1.37%)
occurrences (all)	0	2	2

Non-serious adverse events	Subset nab-paclitaxel + gemcitabine in 2nd line		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 37 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hematoma			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Thromboembolic event			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	10 / 37 (27.03%)		
occurrences (all)	21		
Fever			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Multi-organ failure			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
General status alteration			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Dyspnea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Hypoxia			

subjects affected / exposed occurrences (all) COPD subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all) Pumonary edema subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 1 / 37 (2.70%) 1		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0 1 / 37 (2.70%) 1 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0		
Investigations Weight loss subjects affected / exposed occurrences (all)	 2 / 37 (5.41%) 2		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		
Cardiac disorders Cardiac arrest subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0		

Myocardial infarction subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Hemiparesis subjects affected / exposed occurrences (all) Peripheral motor neuropathy subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 2 / 37 (5.41%) 3 0 / 37 (0.00%) 0 1 / 37 (2.70%) 1		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all) Hemolytic uremic syndrome subjects affected / exposed occurrences (all) Thrombotic thrombocytopenic purpura subjects affected / exposed occurrences (all)	 2 / 37 (5.41%) 2 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0		
Gastrointestinal disorders			

Abdominal pain				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences (all)	2			
Ascites				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Colitis				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Colonic obstruction				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Diarrhea				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences (all)	2			
Gastric ulcer				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Gastroparesis				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences (all)	1			
Gastrointestinal pain				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Ileus				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Mucositis oral				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences (all)	2			

Obstruction gastric subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Diverticulitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Intrapancreatic obstruction subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Hematemesis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Hernia inguinalis with obstruction subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Pancreatitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Small intestinal obstruction subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Stomach pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Colonic perforation subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
Hepatobiliary disorders Bile duct stenosis			

subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Cholecystitis			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	3		
Gallbladder obstruction			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hepatic failure			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Cholestasis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Dilated bile ducts			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Jaundice			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Myalgia			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Biliary tract infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Bladder infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Bronchial infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Catheter related infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Gallbladder infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hepatic infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Lung infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Infection without neutropenia NOS			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		

Paronychia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Pleural infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Sepsis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	9 / 37 (24.32%)		
occurrences (all)	10		
Dehydration			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2014	Amendment to the ICF due to changes to the safety language in the ICF.
26 November 2014	Amendment to add four additional participating institutions.
20 July 2015	Amendment of the protocol to adjust the timing of study procedures, to clarify inclusion/exclusion criteria and increase sample size from 110 to 143 due to observed patient compliance in providing QOL data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 June 2015	Temporary interuption of recruitment at the completion of initial sample size on 18-Jun-2015. The protocol amendment to adjust the timing of study procedures, to clarify inclusion/exclusion criteria and increase sample size from 110 to 143 due to observed patient compliance in providing QOL data was approved on 17-Jul-2015 by the Belgian Health Authority (FAGG) and 20-Jul-2015 by the designated central ethics committee. Recruitment was restarted after all regulatory approvals on 24-Jul-2015.	24 July 2015

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Quality of life endpoints are sensitive to confounding factors such as age, intercurrent disease, time from last completed questionnaire to the last follow-up or death.
Tumour response and AE relationship to treatment were locally assessed.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/8433390

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http://www.ncbi.nlm.nih.gov/pubmed/20724140

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