Clinical trial results:
A prospective randomised controlled phase III trial of gemcitabine and docetaxel compared with doxorubicin as first line treatment in previously untreated advanced unresectable or metastatic soft tissue sarcomas

Summary

EudraCT number	2009-014907-29
Trial protocol	GB
Global end of trial date	08 May 2019

Results information

Result version number	v1 (current)
This version publication date	21 May 2020
First version publication date	21 May 2020
Summary attachment (see zip file)	GeDDiS publication (GeDDiS_publication_LancetOncology_20170904.pdf)

Trial information

Trial identification

Sponsor protocol code	UCL/09/0060

Additional study identifiers

ISRCTN number	ISRCTN07742377
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	UK CTA number: 20363/0285/001-0001, Swiss CTA number: 2013DR3049

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Joint Research Office, Gower Street , London , United Kingdom, WC1E 6BT
Public contact	ctc.sponsor@ucl.ac.uk, University College London, 020 76799264, ctc.geddis@ucl.ac.uk
Scientific contact	ctc.sponsor@ucl.ac.uk, University College London, 020 76799264, ctc.geddis@ucl.ac.uk

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research objective is to compare the efficacy and effectiveness of gemcitabine and docetaxel with that of doxorubicin.

Protection of trial subjects:

The risks for patients in this trial were similar to those for any patient undergoing chemotherapy treatment.
The eligibility criteria were stringent to ensure patients were fit enough to receive treatment, assessments during and after trial treatment were comprehensive and detailed guidance was given in the protocol for dose modifications if/when toxicity from the chemotherapy occurred. Adverse events pertaining to the administration of these drugs were closely monitored throughout the trial. Each patient's GP was informed of their participation and asked to report all serious side effects immediately to the research team at site. Patient cards were also issued to the patients in case of emergencies, which contained information about the trial and contact details of the hospital where they were being treated.
A risk assessment was performed for this trial and an appropriate level of monitoring was carried out, including the monitoring of patient safety.
Safety information was presented to the Trial Management Group, Data Monitoring Committee and Trial Steering Committee on a regular basis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 249
Country: Number of subjects enrolled	Switzerland: 8
Worldwide total number of subjects	257
EEA total number of subjects	249

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	197
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

257 patients were recruited in total, 249 within the United Kingdom and 8 in Switzerland. The trial was opened to recruitment on 25/11/2010, the first patient was recruited on 03/12/2010, the final patient was recruited on 20/01/2014.

Pre-assignment

Screening details:

497 patients were screened.
Patients were excluded due to one of the following reasons: did not meet eligibility criteria, patient decision (declined information sheet, recruitment appointment or randomisation), patient died before enrolment, patient treated at different hospital, clinical decision.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	GemcitabineDocetaxel

Arm description:

Gemcitabine 675 mg/m2 i.v. days 1 and 8, docetaxel 75 mg/m2 i.v. day 8 every three weeks for up to 6 cycles

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

Dosage and administration details:

Gemcitabine 675 mg/m2 i.v. days 1 and 8 every three weeks, for up to 6 cycles

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

Dosage and administration details:

Docetaxel 75 mg/m2 i.v. day 8 every three weeks for up to 6 cycles

Arm title	Doxorubicin

Arm description:

Doxorubicin 75 mg/m2 i.v. day 1 every three weeks for up to 6 cycles

Arm type	Active comparator
Investigational medicinal product name	doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Doxorubicin 75 mg/m2 i.v. day 1 every three weeks for up to 6 cycles

Number of subjects in period 1	GemcitabineDocetaxel	Doxorubicin
Started	128	129
Completed	49	71
Not completed	79	58
Adverse event, serious fatal	1	3
Physician decision	5	4
Consent withdrawn by subject	1	1
death	3	2
other reasons/unknown	11	7
Adverse event, non-fatal	14	1
did not start treatment	2	1
intercurrent illness preventing further treatment	1	1
disease progression	38	34
symptomatic deterioration	3	4

Baseline characteristics

Reporting groups	
Reporting group title	GemcitabineDocetaxel
Reporting group description:	
Gemcitabine 675 mg/m2 i.v. days 1 and 8, docetaxel 75 mg/m2 i.v. day 8 every three weeks for up to 6 cycles	
Reporting group title	Doxorubicin
Reporting group description:	
Doxorubicin 75 mg/m2 i.v. day 1 every three weeks for up to 6 cycles	

Reporting group values	GemcitabineDocetaxel	Doxorubicin	Total
Number of subjects	128	129	257
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)	98	99	197
From 65-84 years	30	30	60
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	77	79	156
Male	51	50	101
WHO performance status Units: Subjects			
0 - Fully active	52	55	107
1 - Ambulatory (work able)	67	63	130
2 - Ambulatory (not work able)	9	11	20
Trojani grade Units: Subjects			
Grade 2	34	29	63
Grade 3	85	85	170
Not known	9	15	24
Histology			
"Other eligible sarcomas" contained 47 non-uterine leiomyosarcoma (23 gemcitabine & docetaxel, 24 doxorubicin).			
Units: Subjects			
Uterine leiomyosarcoma	35	36	71
Synovial sarcoma	6	5	11
Pleomorphic sarcoma	16	16	32
Other eligible sarcomas	71	72	143

End points

End points reporting groups

Reporting group title	GemcitabineDocetaxel
Reporting group description:	
Gemcitabine 675 mg/m2 i.v. days 1 and 8, docetaxel 75 mg/m2 i.v. day 8 every three weeks for up to 6 cycles	
Reporting group title	Doxorubicin
Reporting group description:	
Doxorubicin 75 mg/m2 i.v. day 1 every three weeks for up to 6 cycles	

Primary: Progression free survival at 24 weeks

End point title	Progression free survival at 24 weeks
End point description:	
The primary endpoint for the trial was the proportion of patients who were alive and progression free at 24 weeks post-randomisation. The 24 week Kaplan-Meier progression free survival rates are reported for each arm.	
End point type	Primary
End point timeframe:	
24 weeks after the date of randomisation	

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: percentage				
number (confidence interval 95%)	0.464 (0.375 to 0.548)	0.463 (0.375 to 0.546)		

Statistical analyses

Statistical analysis title	Progression free survival at 24 weeks
Statistical analysis description:	
The sample size was based on a comparison of proportions. As there was censoring before the week 24 time point, Kaplan-Meier rates have been provided and used for the test of proportions in this section. The following are the results if we remove censored patients and perform a standard test of proportions: Doxorubicin: 59/127 progression free - 46.5% (37.7% - 55.2%) Gemcitabine & Docetaxel: 57/123 progression free - 46.3% (37.4% - 55.3%) p=0.99. Conclusions are the same.	
Comparison groups	GemcitabineDocetaxel v Doxorubicin

Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99 [1]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.123
upper limit	0.121

Notes:

[1] - Conclusions are exactly the same if we do a standard test of proportions or using the K-M rates as we have here.

Secondary: Progression free survival at 12 weeks

End point title	Progression free survival at 12 weeks

End point description:

The 12 week Kaplan-Meier progression free survival rates are reported for each arm.

End point type	Secondary

End point timeframe:

12 weeks from date of randomisation.

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: percentage				
number (confidence interval 95%)	0.638 (0.548 to 0.715)	0.721 (0.635 to 0.790)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

Kaplan-Meier median progression free survival rates are reported for each arm as well as the hazard ratio comparing the two arms.

End point type	Secondary

End point timeframe:

Entire follow up period.

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: weeks				
median (confidence interval 95%)	23.7 (18.1 to 28.0)	23.3 (19.6 to 30.4)		

Statistical analyses

Statistical analysis title	PFS hazard ratio

Statistical analysis description:

Hazard ratio comparing PFS curves (Gemcitabine & Docetaxel vs Doxorubicin).

The hazard ratio reported is from an unadjusted comparison. After adjusting for histological subtype, the HR was 1·26 (0·97–1·63; p=0·08).

Comparison groups	GemcitabineDocetaxel v Doxorubicin
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.65

Secondary: Overall survival

End point title	Overall survival

End point description:

The median overall survival Kaplan-Meier estimates are reported for each arm as well as the hazard ratio comparing the two curves.

End point type	Secondary

End point timeframe:

Entire follow up period.

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: weeks				
median (confidence interval 95%)	67.3 (53.1 to 83.1)	76.3 (60.0 to 91.3)		

Statistical analyses

Statistical analysis title	OS hazard ratio

Statistical analysis description:

Hazard ratio comparing OS curves (Gemcitabine & Docetaxel vs Doxorubicin). The hazard ratio reported is from an unadjusted comparison.

Comparison groups	GemcitabineDocetaxel v Doxorubicin
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.57

Secondary: Objective response by RECIST 1.1

End point title	Objective response by RECIST 1.1

End point description:

End point type	Secondary

End point timeframe:

Patients were assessed at 12 weeks post-randomisation, 24 weeks post-randomisation and then approximately every 12 weeks until disease progression or 24 months post-randomisation.

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: patients				
Complete Response (CR)	0	2		
Partial Response (PR)	25	23		
Stable Disease (SD)	50	60		
Progressive Disease (PD)	27	25		
Not Evaluable	26	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life at 12 weeks

End point title	Quality of life at 12 weeks

End point description:

Here we report details of the difference between treatment arms in Global Health Status score at 12 weeks.

Further details of differences in quality of life at 12 weeks were reported in the main trial paper. There was no evidence to suggest that quality of life measures differed between the two treatment groups.

End point type	Secondary

End point timeframe:

12 weeks post-randomisation.

End point values	GemcitabineDocetaxel	Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	64		
Units: score				
arithmetic mean (standard deviation)	59.1 (± 21.8)	63.8 (± 22.5)		

Statistical analyses

Statistical analysis title	Difference in mean Global Health Status score

Statistical analysis description:

From a linear regression model, adjusting for baseline score, histological subtype, and time since baseline.

Treatment effect is calculated as: (gemcitabine and docetaxel change from baseline) – (doxorubicin change from baseline).

Comparison groups	GemcitabineDocetaxel v Doxorubicin
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-5.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	4.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (including serious adverse events) that occurred between informed consent and 30 days post last trial treatment administration were recorded.

Adverse event reporting additional description:

Adverse events pertaining to the trial drugs were closely monitored throughout the trial. Each patients GP was informed of their participation and asked to report all serious side effects immediately to sites. Patient contact cards and adverse event diaries were also issued to patients and reviewed before each treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	GemcitabineDocetaxel

Reporting group description:

Gemcitabine 675 mg/m2 i.v. days 1 and 8, docetaxel 75 mg/m2 i.v. day 8 every three weeks for up to 6 cycles

Reporting group title	Doxorubicin

Reporting group description:

Doxorubicin 75 mg/m2 i.v. day 1 every three weeks for up to 6 cycles

Serious adverse events	GemcitabineDocetaxel	Doxorubicin	
Total subjects affected by serious adverse events			
subjects affected / exposed	71 / 126 (56.35%)	69 / 128 (53.91%)	
number of deaths (all causes)	80	74	
number of deaths resulting from adverse events	3	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hot flashes			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			

subjects affected / exposed	4 / 126 (3.17%)	9 / 128 (7.03%)	
occurrences causally related to treatment / all	1 / 4	5 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Oedema limbs			
subjects affected / exposed	2 / 126 (1.59%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	15 / 126 (11.90%)	14 / 128 (10.94%)	
occurrences causally related to treatment / all	10 / 19	13 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 126 (1.59%)	4 / 128 (3.13%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death NOS			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Immune system disorders			
Bronchial infection			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	5 / 126 (3.97%)	3 / 128 (2.34%)	
occurrences causally related to treatment / all	0 / 5	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			

subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	10 / 126 (7.94%)	18 / 128 (14.06%)	
occurrences causally related to treatment / all	10 / 10	22 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Chest pain - cardiac			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular systolic dysfunction			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Seizure			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 126 (0.00%)	2 / 128 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 126 (3.17%)	6 / 128 (4.69%)	
occurrences causally related to treatment / all	4 / 4	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	15 / 126 (11.90%)	26 / 128 (20.31%)	
occurrences causally related to treatment / all	14 / 15	26 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 126 (3.17%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	1 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bloating			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colonic ulcer			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 126 (0.79%)	4 / 128 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	9 / 126 (7.14%)	5 / 128 (3.91%)	
occurrences causally related to treatment / all	7 / 9	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	2 / 126 (1.59%)	4 / 128 (3.13%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	5 / 126 (3.97%)	3 / 128 (2.34%)	
occurrences causally related to treatment / all	2 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin reaction	Additional description: reaction at Hickman line site		
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulceration			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			

subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anorectal infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection	Additional description: Hickman line infection		
alternative dictionary used: MedDRA 21			

subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	5 / 126 (3.97%)	5 / 128 (3.91%)	
occurrences causally related to treatment / all	2 / 5	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 126 (0.79%)	2 / 128 (1.56%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	1 / 1	1 / 1	
Cellulitis			
subjects affected / exposed	2 / 126 (1.59%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin infection			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory infection			
subjects affected / exposed	3 / 126 (2.38%)	3 / 128 (2.34%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 126 (1.59%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	GemcitabineDocetaxel	Doxorubicin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 126 (100.00%)	128 / 128 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Tumour pain			
subjects affected / exposed	3 / 126 (2.38%)	2 / 128 (1.56%)	
occurrences (all)	3	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 126 (0.79%)	2 / 128 (1.56%)	
occurrences (all)	1	2	
Thromboembolic event			
subjects affected / exposed	4 / 126 (3.17%)	8 / 128 (6.25%)	
occurrences (all)	4	8	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	108 / 126 (85.71%)	116 / 128 (90.63%)	
occurrences (all)	108	116	
Pain			
subjects affected / exposed	79 / 126 (62.70%)	80 / 128 (62.50%)	
occurrences (all)	79	80	
Fever			
subjects affected / exposed	28 / 126 (22.22%)	25 / 128 (19.53%)	
occurrences (all)	28	25	
Oedema limbs			
subjects affected / exposed	55 / 126 (43.65%)	24 / 128 (18.75%)	
occurrences (all)	55	24	
Non-cardiac chest pain			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences (all)	2	1	
Infusion related reaction			
subjects affected / exposed	5 / 126 (3.97%)	0 / 128 (0.00%)	
occurrences (all)	5	0	
Sudden death NOS			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	4 / 126 (3.17%)	1 / 128 (0.78%)	
occurrences (all)	4	1	

Anaphylaxis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Premature menopause			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	26 / 126 (20.63%)	24 / 128 (18.75%)	
occurrences (all)	26	24	
Dyspnoea			
subjects affected / exposed	29 / 126 (23.02%)	19 / 128 (14.84%)	
occurrences (all)	29	19	
Pneumonitis			
subjects affected / exposed	8 / 126 (6.35%)	4 / 128 (3.13%)	
occurrences (all)	8	4	
Epistaxis			
subjects affected / exposed	13 / 126 (10.32%)	2 / 128 (1.56%)	
occurrences (all)	13	2	
Hiccups			
subjects affected / exposed	3 / 126 (2.38%)	2 / 128 (1.56%)	
occurrences (all)	3	2	
Pleural effusion			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences (all)	2	1	
Bronchopulmonary haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Pneumothorax			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	10 / 126 (7.94%)	10 / 128 (7.81%)	
occurrences (all)	10	10	
Investigations			
White blood cell decreased			
subjects affected / exposed	63 / 126 (50.00%)	43 / 128 (33.59%)	
occurrences (all)	63	43	
Neutrophil count decreased			
subjects affected / exposed	71 / 126 (56.35%)	58 / 128 (45.31%)	
occurrences (all)	71	58	
Platelet count decreased			
subjects affected / exposed	31 / 126 (24.60%)	14 / 128 (10.94%)	
occurrences (all)	31	14	
Alkaline phosphatase increased			
subjects affected / exposed	48 / 126 (38.10%)	43 / 128 (33.59%)	
occurrences (all)	48	43	
Alanine aminotransferase increased			
subjects affected / exposed	37 / 126 (29.37%)	35 / 128 (27.34%)	
occurrences (all)	37	35	
Aspartate aminotransferase increased			
subjects affected / exposed	13 / 126 (10.32%)	14 / 128 (10.94%)	
occurrences (all)	13	14	
GGT increased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Urea increased			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	12 / 126 (9.52%)	11 / 128 (8.59%)	
occurrences (all)	12	11	
Blood creatinine decreased			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Vascular access complication			
subjects affected / exposed	1 / 126 (0.79%)	2 / 128 (1.56%)	
occurrences (all)	1	2	
Fracture			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Radiation recall reaction (dermatologic)			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Chest pain - cardiac			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences (all)	2	1	
Heart failure			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Left ventricular systolic dysfunction			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Myocardial infarction			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences (all)	1	1	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	25 / 126 (19.84%)	24 / 128 (18.75%)	
occurrences (all)	25	24	
Peripheral sensory neuropathy			
subjects affected / exposed	31 / 126 (24.60%)	14 / 128 (10.94%)	
occurrences (all)	31	14	
Dizziness			
subjects affected / exposed	4 / 126 (3.17%)	10 / 128 (7.81%)	
occurrences (all)	4	10	
Syncope			
subjects affected / exposed	0 / 126 (0.00%)	3 / 128 (2.34%)	
occurrences (all)	0	3	
Tremor			

subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	112 / 126 (88.89%)	101 / 128 (78.91%)	
occurrences (all)	112	101	
Febrile neutropenia			
subjects affected / exposed	15 / 126 (11.90%)	26 / 128 (20.31%)	
occurrences (all)	15	26	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	72 / 126 (57.14%)	87 / 128 (67.97%)	
occurrences (all)	72	87	
Mucositis oral			
subjects affected / exposed	61 / 126 (48.41%)	82 / 128 (64.06%)	
occurrences (all)	61	82	
Constipation			
subjects affected / exposed	51 / 126 (40.48%)	55 / 128 (42.97%)	
occurrences (all)	51	55	
Diarrhoea			
subjects affected / exposed	52 / 126 (41.27%)	50 / 128 (39.06%)	
occurrences (all)	52	50	
Vomiting			
subjects affected / exposed	32 / 126 (25.40%)	49 / 128 (38.28%)	
occurrences (all)	32	49	
Dyspepsia			
subjects affected / exposed	18 / 126 (14.29%)	28 / 128 (21.88%)	
occurrences (all)	18	28	
Abdominal pain			
subjects affected / exposed	16 / 126 (12.70%)	20 / 128 (15.63%)	
occurrences (all)	16	20	
Dry mouth			
subjects affected / exposed	5 / 126 (3.97%)	12 / 128 (9.38%)	
occurrences (all)	5	12	
Rectal haemorrhage			

subjects affected / exposed	3 / 126 (2.38%)	1 / 128 (0.78%)	
occurrences (all)	3	1	
Colonic ulcer			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Abdominal distension			
subjects affected / exposed	5 / 126 (3.97%)	0 / 128 (0.00%)	
occurrences (all)	5	0	
Ascites			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Small intestinal obstruction			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Rectal tenesmus			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Intestinal perforation			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	95 / 126 (75.40%)	110 / 128 (85.94%)	
occurrences (all)	95	110	
Urticaria			
subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences (all)	1	1	
Skin ulceration			
subjects affected / exposed	3 / 126 (2.38%)	0 / 128 (0.00%)	
occurrences (all)	3	0	
Rash			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	16 / 126 (12.70%)	3 / 128 (2.34%)	
occurrences (all)	16	3	
Lichen sclerosus			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Night sweats			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Renal vein thrombosis			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 126 (9.52%)	12 / 128 (9.38%)	
occurrences (all)	12	12	
Myalgia			
subjects affected / exposed	12 / 126 (9.52%)	5 / 128 (3.91%)	
occurrences (all)	12	5	

Muscle weakness lower limb			
subjects affected / exposed	2 / 126 (1.59%)	2 / 128 (1.56%)	
occurrences (all)	2	2	
Bone pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	8 / 126 (6.35%)	9 / 128 (7.03%)	
occurrences (all)	8	9	
Lower respiratory tract infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	6 / 126 (4.76%)	4 / 128 (3.13%)	
occurrences (all)	6	4	
Varicella zoster virus infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	3 / 128 (2.34%)	
occurrences (all)	0	3	
Nail infection			
subjects affected / exposed	1 / 126 (0.79%)	2 / 128 (1.56%)	
occurrences (all)	1	2	
Lung infection			
subjects affected / exposed	4 / 126 (3.17%)	5 / 128 (3.91%)	
occurrences (all)	4	5	
Upper respiratory infection			
subjects affected / exposed	2 / 126 (1.59%)	2 / 128 (1.56%)	
occurrences (all)	2	2	
Infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	3 / 126 (2.38%)	1 / 128 (0.78%)	
occurrences (all)	3	1	
Skin infection			
subjects affected / exposed	2 / 126 (1.59%)	1 / 128 (0.78%)	
occurrences (all)	2	1	
Wound infection			

subjects affected / exposed	1 / 126 (0.79%)	1 / 128 (0.78%)	
occurrences (all)	1	1	
Device related infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	4 / 126 (3.17%)	0 / 128 (0.00%)	
occurrences (all)	4	0	
Bronchial infection			
subjects affected / exposed	3 / 126 (2.38%)	0 / 128 (0.00%)	
occurrences (all)	3	0	
Catheter related infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Escherichia infection			
alternative dictionary used: MedDRA 21			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	1 / 126 (0.79%)	2 / 128 (1.56%)	
occurrences (all)	1	2	
Anal abscess			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Stoma site abscess			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	56 / 126 (44.44%)	63 / 128 (49.22%)	
occurrences (all)	56	63	
Hypoalbuminaemia			

subjects affected / exposed	40 / 126 (31.75%)	28 / 128 (21.88%)	
occurrences (all)	40	28	
Hyponatraemia			
subjects affected / exposed	25 / 126 (19.84%)	20 / 128 (15.63%)	
occurrences (all)	25	20	
Hyperkalaemia			
subjects affected / exposed	18 / 126 (14.29%)	11 / 128 (8.59%)	
occurrences (all)	18	11	
Hypokalaemia			
subjects affected / exposed	8 / 126 (6.35%)	9 / 128 (7.03%)	
occurrences (all)	8	9	
Hyperglycaemia			
subjects affected / exposed	3 / 126 (2.38%)	1 / 128 (0.78%)	
occurrences (all)	3	1	
Hypercalcaemia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 128 (0.78%)	
occurrences (all)	0	1	
Electrolyte imbalance			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	
Fluid retention			
alternative dictionary used: MedDRA 22.1			
subjects affected / exposed	1 / 126 (0.79%)	0 / 128 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2011	Protocol: Update on contraception requirements Clarification on dose modifications for haematological toxicity PIS: Clarification of timepoints for CT/MRI scans, and radiation risk to patients Clarification that consent to allow genetic testing on research blood & tissue samples is optional
21 October 2011	Protocol - Inclusion criteria: Histological confirmation wording changed to clarify high grade disease Chemotherapy wording changed to clarify no previous chemotherapy for sarcoma and no doxorubicin for any previous cancer ALP wording clarified
08 March 2013	Protocol: Addition of secondary endpoint (Time from start of treatment to progression or death (whichever occurs first))
23 March 2016	Protocol: Addition of guidance to allow patients who have not progressed after 24 months on trial be scanned according to local site practice
25 January 2019	Protocol: Translational Research section updated to include information on some additional exploratory research that is planned to be performed on the stored blood and tissue samples

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Non-serious AEs: includes SAEs and non-serious AEs
Non-serious AEs: highest grade experienced by patients collected, therefore 'subjects affected' number has been entered in 'occurrences'

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28882536