Clinical trial results:
A phase II randomized – non comparative – study on the activity of trabectedin or gemcitabine + docetaxel in metastatic or locally relapsed uterine leiomyosarcoma pretreated with conventional chemotherapy.

Summary

EudraCT number	2009-016017-24
Trial protocol	IT
Global end of trial date	30 April 2017

Results information

Result version number	v1 (current)
This version publication date	22 July 2022
First version publication date	22 July 2022

Trial information

Trial identification

Sponsor protocol code	2009-016017-24

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02249702
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Istituto di Ricerche Farmacologiche Mario Negri IRCCS
Sponsor organisation address	Via Mario Negri 2, Milan, Italy, 20156
Public contact	Eliana Rulli, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, 039 0239014645, eliana.rulli@marionegri.it
Scientific contact	Eliana Rulli, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, 039 0239014645, eliana.rulli@marionegri.it

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	11 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2017
Global end of trial reached?	Yes
Global end of trial date	30 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective will be to assess the clinical benefit rate (defined as 6-month progression free rate) with T in patients with locally relapsed/metastatic uterine leiomyosarcoma pretreated with anthracycline ± ifosfamide and/or gemcitabine ± docetaxel. For the subgroup population pretreated only with anthracycline ± ifosfamide the patients enrolled in the arm B will serve as a parallel internal control.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 168
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	137
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

To be eligible for the trial patients must have received at least one line of chemotherapy either in adjuvant setting or as first line chemotherapy in advanced/recurrent disease. Patients who have not already received gemcitabine ± docetaxel will be randomized to receive trabectedin (arm A) or gemcitabine+docetaxel (arm B).

Pre-assignment

Screening details:

NA

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Trabectedin (Arm A randomized)

Arm description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

Arm type	Experimental
Investigational medicinal product name	Trabectedin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Trabectedin is manufactured by PharmaMar as a lyophilized powder in glass vials containing 0.25 or 1 mg of the drug. It has to be reconstituted in 5 ml or 20 ml of sterile water for injection and further diluted in sodium chloride solution 0.9% for a total volume of 500 ml and administered at the dose of 1.3 mg/sqm as a 24-hour continuous infusion via a central venous access. All patients must have an indwelling central catheter at the time of starting trabectedin.

Arm title	Gemcitabine+Docetaxel (Arm B)

Arm description:

Gemcitabine+docetaxel treatment is planned for six cycles, unless there is evidence of disease progression, unacceptable toxicity or patient's intolerance or unwillingness to continue treatment, or medical decision by the responsible physician. Patients with continued response after six cycles can receive two additional cycles of combination therapy or continue with Gemcitabine alone.

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine+Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients will receive gemcitabine 900 mg/m2 on days 1 and 8 intravenously over 90 min, followed by docetaxel 75 mg/m2 on day 8 intravenously over 1 h.

Arm title	Trabectedin (Arm A)

Arm description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

Arm type	Experimental
Investigational medicinal product name	Trabectedin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Trabectedin is manufactured by PharmaMar as a lyophilized powder in glass vials containing 0.25 or 1 mg of the drug. It has to be reconstituted in 5 ml or 20 ml of sterile water for injection and further diluted in sodium chloride solution 0.9% for a total volume of 500 ml and administered at the dose of 1.3 mg/sqm as a 24-hour continuous infusion via a central venous access. All patients must have an indwelling central catheter at the time of starting trabectedin.

Number of subjects in period 1	Trabectedin (Arm A randomized)	Gemcitabine+Docetaxel (Arm B)	Trabectedin (Arm A)
Started	45	42	81
Completed	45	42	81

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	168	168	
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)	137	137	
From 65-84 years	31	31	
85 years and over	0	0	
Age continuous Units: years			
median	56.2		
inter-quartile range (Q1-Q3)	49.4 to 63.1	-	
Gender categorical Units: Subjects			
Female	168	168	

Subject analysis sets	
Subject analysis set title	Safety set A
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were assigned to trabectedin arm, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

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

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were assigned to trabectedin arm, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

Subject analysis set title	PP set A
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were assigned to trabectedin arm, without major violations of eligibility criteria, who have received at least two cycles of treatment.

Subject analysis set title	PP set B
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were assigned to trabectedin arm, without major violations of eligibility criteria, who have received at least two cycles of treatment.

Subject analysis set title	Safety set A (randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were randomized to one of the treatment arms, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

Subject analysis set title	PP set A (randomized)
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were randomized to one of the treatment arms, without major violations of eligibility criteria, who have received at least two cycle of the treatment assigned.

Reporting group values	Safety set A	Safety set B	PP set A
Number of subjects	123	39	115
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)	100	34	94
From 65-84 years	23	5	21
85 years and over	0	0	0
Age continuous Units: years			
median	56.6	54.1	56.6
inter-quartile range (Q1-Q3)	50.5 to 63.4	45.4 to 61.9	50.4 to 63.2
Gender categorical Units: Subjects			
Female	123	39	115

Reporting group values	PP set B	Safety set A (randomized)	PP set A (randomized)
Number of subjects	38	43	39
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	33		
From 65-84 years	5		
85 years and over	0		

Age continuous Units: years median inter-quartile range (Q1-Q3)	 54.7 45.4 to 61.9		
Gender categorical Units: Subjects			
Female	38		

End points

End points reporting groups

Reporting group title	Trabectedin (Arm A randomized)

Reporting group description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

Reporting group title	Gemcitabine+Docetaxel (Arm B)

Reporting group description:

Gemcitabine+docetaxel treatment is planned for six cycles, unless there is evidence of disease progression, unacceptable toxicity or patient's intolerance or unwillingness to continue treatment, or medical decision by the responsible physician. Patients with continued response after six cycles can receive two additional cycles of combination therapy or continue with Gemcitabine alone.

Reporting group title	Trabectedin (Arm A)

Reporting group description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

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

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were assigned to trabectedin arm, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

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

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were assigned to trabectedin arm, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

Subject analysis set title	PP set A
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were assigned to trabectedin arm, without major violations of eligibility criteria, who have received at least two cycles of treatment.

Subject analysis set title	PP set B
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were assigned to trabectedin arm, without major violations of eligibility criteria, who have received at least two cycles of treatment.

Subject analysis set title	Safety set A (randomized)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population includes all subjects who provided informed consent and were randomized to one of the treatment arms, who had no major violations of eligibility criteria, and who received at least one dose of treatment.

Subject analysis set title	PP set A (randomized)
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population includes all subjects who provided informed consent and were randomized to one of the treatment arms, without major violations of eligibility criteria, who have received at least two cycle of the treatment assigned.

Primary: PFS-6 (Arm A)

End point title	PFS-6 (Arm A)[1]

End point description:

PFS-6 was defined as the percentage of patients included in the PP population who were alive and progression free at 6 months after randomization.

End point type	Primary

End point timeframe:

6 months

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Trabectedin (Arm A)	PP set A		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	81	108		
Units: patients	38	38		

Statistical analyses

Statistical analysis title	Progression Free Survival at 6 months (Arm A)
Comparison groups	Trabectedin (Arm A) v PP set A
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	superiority[2]
Parameter estimate	Proportion of responder
Point estimate	35.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	26.2
upper limit	45

Notes:

[2] - Since the trail was non-comparative, no statistical comparison between arms was planned and performed

Primary: PFS-6 (Arm B)

End point title	PFS-6 (Arm B)[3]

End point description:

PFS-6 was defined as the percentage of patients included in the PP population who were alive and progression free at 6 months after randomization.

End point type	Primary

End point timeframe:

6 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Gemcitabine+Docetaxel (Arm B)	PP set B		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	33	33		
Units: patients	17	17		

Statistical analyses

Statistical analysis title	Progression Free Survival at 6 months (Arm B)
Comparison groups	Gemcitabine+Docetaxel (Arm B) v PP set B
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Proportion of responder
Point estimate	51.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	33.5
upper limit	69.2

Primary: PFS-6 (Arm A randomized)

End point title	PFS-6 (Arm A randomized)[4]

End point description:

PFS-6 was defined as the percentage of patients included in the PP population who were alive and progression free at 6 months after randomization.

End point type	Primary

End point timeframe:

6 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Trabectedin (Arm A randomized)	PP set A (randomized)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	38	38		
Units: patients	13	13		

Statistical analyses

Statistical analysis title	Progression Free Survival at 6 months (Arm A rand)
Comparison groups	Trabectedin (Arm A randomized) v PP set A (randomized)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Proportion of responder
Point estimate	34.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.6
upper limit	51.4

Secondary: PFS (Arm A)

End point title	PFS (Arm A)[5]

End point description:

PFS was defined as the time from the date of randomization/registration to the date of first progression or death from any cause, whichever comes first.

End point type	Secondary

End point timeframe:

From randomization/registration

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Trabectedin (Arm A)	PP set A		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	81	115		
Units: months				
median (inter-quartile range (Q1-Q3))	4.1 (1.9 to 10.7)	4.1 (1.9 to 10.7)		

Statistical analyses

Statistical analysis title	Progression Free Survival (Arm A)
Comparison groups	Trabectedin (Arm A) v PP set A
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Median PFS
Point estimate	4.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	5.7

Notes:

[6] - Since the trail was non-comparative, no statistical comparison between arms was planned and performed

Secondary: PFS (Arm A randomized)

End point title	PFS (Arm A randomized)[7]

End point description:

PFS was defined as the time from the date of randomization/registration to the date of first progression or death from any cause, whichever comes first.

End point type	Secondary

End point timeframe:

From the date of randomization/registration

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Trabectedin (Arm A randomized)	PP set A (randomized)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	39	39		
Units: months				
median (inter-quartile range (Q1-Q3))	3.5 (1.7 to 8.6)	3.5 (1.7 to 8.6)		

Statistical analyses

Statistical analysis title	Progression Free Survival (Arm A randomized)
Comparison groups	Trabectedin (Arm A randomized) v PP set A (randomized)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median PFS
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	7

Secondary: PFS (Arm B)

End point title	PFS (Arm B)[8]

End point description:

PFS was defined as the time from the date of randomization/registration to the date of first progression or death from any cause, whichever comes first.

End point type	Secondary

End point timeframe:

From the date of randomization/registration

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the trail was non-comparative, no statistical comparison between arms was planned and performed

End point values	Gemcitabine+Docetaxel (Arm B)	PP set B		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	38	38		
Units: months				
median (inter-quartile range (Q1-Q3))	6.9 (2.4 to 15.4)	6.9 (2.4 to 15.4)		

Statistical analyses

Statistical analysis title	Progression Free Survival (Arm B)
Comparison groups	Gemcitabine+Docetaxel (Arm B) v PP set B
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median PFS
Point estimate	6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.6
upper limit	14.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the study

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Trabectedin (Arm A randomized)

Reporting group description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

Reporting group title	Gemcitabine+Docetaxel (Arm B)

Reporting group description:

Gemcitabine+docetaxel treatment is planned for six cycles, unless there is evidence of disease progression, unacceptable toxicity or patient's intolerance or unwillingness to continue treatment, or medical decision by the responsible physician. Patients with continued response after six cycles can receive two additional cycles of combination therapy or continue with Gemcitabine alone.

Reporting group title	Trabectedin (Arm A)

Reporting group description:

Trabectedin treatment can be continued until progressive disease, major toxicity, patient's intolerance or unwillingness to continue treatment or medical decision by the responsible physician.

Serious adverse events	Trabectedin (Arm A randomized)	Gemcitabine+Docetaxel (Arm B)	Trabectedin (Arm A)
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 45 (57.78%)	26 / 42 (61.90%)	0 / 126 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Pulmonary thrombosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	1 / 45 (2.22%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 45 (2.22%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	0 / 45 (0.00%)	2 / 42 (4.76%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alkaline			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Injection site reaction			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 45 (4.44%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 45 (4.44%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 42 (4.76%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)	2 / 42 (4.76%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			

subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			

subjects affected / exposed	0 / 45 (0.00%)	1 / 42 (2.38%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 42 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Trabectedin (Arm A randomized)	Gemcitabine+Docetaxel (Arm B)	Trabectedin (Arm A)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 45 (100.00%)	42 / 42 (100.00%)	126 / 126 (100.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 45 (15.56%)	12 / 42 (28.57%)	29 / 126 (23.02%)
occurrences (all)	27	23	100
Myalgia			
subjects affected / exposed	7 / 45 (15.56%)	7 / 42 (16.67%)	12 / 126 (9.52%)
occurrences (all)	33	16	86
Blood and lymphatic system disorders			
ALT increased			
subjects affected / exposed	11 / 45 (24.44%)	5 / 42 (11.90%)	16 / 126 (12.70%)
occurrences (all)	54	16	44
Haemoglobin			
subjects affected / exposed	19 / 45 (42.22%)	31 / 42 (73.81%)	24 / 126 (19.05%)
occurrences (all)	71	103	73
Leucocytes/WBC			
subjects affected / exposed	22 / 45 (48.89%)	20 / 42 (47.62%)	26 / 126 (20.63%)
occurrences (all)	55	53	73
Neutrophils/granulocytes			
subjects affected / exposed	25 / 45 (55.56%)	21 / 42 (50.00%)	27 / 126 (21.43%)
occurrences (all)	57	51	72
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	12 / 45 (26.67%) 19	12 / 42 (28.57%) 21	32 / 126 (25.40%) 75

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported