



Clinical trial results: *Salvage therapy with trabectedin in metastatic pancreatic adenocarcinoma: a single-arm phase II trial*

Summary

EudraCT number*	2010-024287-17
Trial protocol	PACT-18
Global end of trial date*	31Mar2013

Trial information

Trial identification

Sponsor protocol code*	PACT-18
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01339754
WHO universal trial number (UTN)	-

Notes:

Sponsors details*

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	reni.michele@hsr.it
Scientific contact	reni.michele@hsr.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

Results analysis stage

Analysis stage*	Final
Date of interim/final analysis*	Dec 2012
Is this the analysis of the primary completion data?*	Yes
Global end of trial reached?*	Yes
Global end of trial date*	31Mar2013
Was the trial ended prematurely?	No

General information about the trial

Main objective of the trial*: to assess the therapeutic activity of trabectedin in terms of progression-free survival rate at 6 months from treatment start in patients with metastatic pancreatic adenocarcinoma

Actual start date of recruitment*	01Feb2011
Long term follow-up planned*	Yes
If Yes, rationale:	Safety <u>Efficacy</u> Ethical reason Regulatory reason Scientific research
Duration	Years
Independent data monitoring committee (IDMC) involvement?*	No
Protection of trial subjects*:	Yes
Background therapy:	No
Evidence for comparator:	

Population of trial subjects**Subjects enrolled per country**

Country:	Italy
Planned number of subjects	25
Actual Number of subjects enrolled*	25
Worldwide total number of subjects	0
EEA total number of subjects	25 (only in Italy)

Subjects enrolled per age group

In utero*	N/A
Preterm newborn - gestational age < 37wks*	N/A
Newborns (0-27 days)*	N/A
Infants and toddlers (28 days-23months)*	N/A
Children (2-11 years)*	N/A
Adolescents (12-17 years)*	N/A
Adults (18-64 years)*	18
From 65 to 84 years*	7
85 years and over*	0

Subject disposition

Recruitment details:

Enrollment from 01Feb2011 to 25Jan2012 in 1 clinical center

Pre-assignment - Screening details:

The study population consists of adult Caucasian patients (≥ 18 years old) affected by pancreatic cancer

Inclusion criteria

- ◆ Histologically or cytologically confirmed diagnosis of pancreatic adenocarcinoma
- ◆ Metastatic pancreatic cancer (Stage IV) progressed after first line gemcitabine-based chemotherapy
- ◆ Age ≥ 18 and ≤ 75 years
- ◆ Karnofsky performance status >50
- ◆ Measurable disease according to RECIST criteria
- ◆ Adequate bone marrow, liver and kidney function
- ◆ Written informed consent
- ◆ Adequate contraceptive methods for the patient and patient partners

Exclusion criteria

- ◆ Previous second line chemotherapy
- ◆ Concurrent treatment with other experimental drugs
- ◆ Symptomatic brain metastasis
- ◆ Severe comorbidities (e.g. cardiac diseases, history of psychiatric disabilities)
- ◆ Prior or concurrent malignancies at other sites with the exception of surgically cured carcinoma in-situ of the cervix and basal or squamous cell carcinoma of the skin and of other neoplasms without evidence of disease at least from 5 years
- ◆ Pregnancy or lactation.
- ◆ Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- ◆ More than 1 prior chemo line

Period 1

Period title*	<i>Overall Trial</i>
Is this the baseline period?	No
Allocation method*	Non Randomised
Blinding used*	

Arms

Arm title*	Trabectedin
Arm description:	Trabectedin 1.3 mg/m ²
Arm type*	Experimental
Investigational medicinal product name*	TRABECTEDIN
Investigational medicinal product code	
Other name	

Pharmaceutical forms*	VIALS
Routes of administration*	INTRAVENOUS
Dosage and administration details*	1.3 mg/m ² as a 3h intravenous continuous infusion every 3 weeks

Number of subjects in period	TRABECTEDIN	
Started*	25	
Completed*	1	
Subject non-completion reason (if applicable)		
AE, non fatal	0	
AE, fatal	0	
Consent withdrawn by subject	0	
Lack of efficacy	24	
Lost to follow up	0	
Physician decision	0	
Pregnancy	0	
Protocol Deviation		
Other		

Baseline characteristics

Reporting groups* Overall cohort

Reporting group title*	TRABECTEDIN
Number of subjects at the baseline*	25 patients

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	TRABECTEDIN
Subject analysis set type*	Intention to treat
Subject analysis set description*	<i>Patient assigned to treatment who followed the study protocol without significant violations</i>
Number of subjects in subjects analysis set*	25

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical			

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	Overall cohort	Years	Median 59.6 years	full range (min-max) 48.3-73.8 years

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	Gender	Count	Female: 17 Male: 8

Study specific characteristics

	Characteristic title*	Units*	Categories*	Number of subject for each categories
Study specific categorical	Karnofsky Performance status	count	70-80, 90-100	70-80 (9) 90-100 (16)
Study specific categorical	Metastases site	count	Liver, Lung	Liver (20) Lung (12)

Study specific categorical	Median CA 19.9	count	>UNL, < UNL	> UNL (20) < UNL (5)
Study specific categorical				
Study specific categorical				

End points

Add subject analysis set if you wish to report on groups different from reporting groups defined above

Subject analysis set title*	TRABECTEDIN
Subject analysis set type*	Per protocol
Subject analysis set description*	Patient assigned to ARM A (PEXG+Metformin) treatment who followed the study protocol without significant violations
Number of subject in subject analysis set *	25

End points definitions

End point title*	6 Months Progression Free Survival (PFS-6)	
		Values
Countable or measurable?*	Measurable	Median PFS-6
If countable, Countable units*:		
If measurable, Measurable units*	Months	
Measure type*:	Median	
Precision/dyspersion type*	95% Confidence Interval (CI)	

End point type* Primary

End point timeframe*: From start of therapy to 6 months after

End point title*	Overall survival	
		Values
Countable or measurable?*	Measurable	Median overall survival
If countable, Countable units*:		
If measurable, Measurable units*	Months	
Measure type*:	Median	
Precision/dyspersion type*	95% Confidence Interval (CI)	

End point type* Secondary

End point timeframe*: From start of therapy to death from any cause

End point title*	Objective Response Rate	
		Values
Countable or measurable?*	Countable	Proportion of patients with partial response

If countable, Countable units*:	Percentage (%)	
If measurable, Measurable units*:		
Measure type*:	Number	
Precision/dyspersion type*:	None	

End point type*	Secondary
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End point timeframe*: During study treatment period
 Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Trabectedin		
Period	Study Treatment Period		
Arms	N/A		
subject analysis sets	Per protocol		

Adverse events

Adverse events information

Timeframe for reporting adverse events*: *Enter the time point(s) or time period for AE assessment*

From ICF signature to 28 days after last study drug infusion

First patient first visit: 01Feb2011

Last recruitment date: 25Jan2012

Study closure: 31Mar2013

Adverse event reporting additional description: *Adverse events (AEs) were collected systematically throughout the study. Patients were assessed for AEs at each study visit, and AEs were monitored continuously. The severity of AEs was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Serious Adverse Events (SAEs) were reported immediately to the study sponsor and Ethics Committee*

Assessment type*	Systematic
Frequency threshold for reporting non-serious adverse events*	Typically, non-serious AEs are reported if they occur in more than 5% of subjects in any treatment group

Dictionary used

Dictionary name*	CTCAE
Dictionary version*	3.0

Adverse events reporting group definition

Use arms from baseline period as reporting groups

OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	25
Subjects affected by non -SAE*	25
Total number of deaths (all causes)*	23
Total number of deaths resulting from adverse event*	0

Serious adverse event details and values

System organ class*: Neurology, Pulmonary/Upper Respiratory, Blood/Bone Marrow, Gastrointestinal

Event term*: Transient Ischemic attack, Respiratory Failure, Febrile Neutropenia, Ulcerative Esophagitis

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number
Trabectedin	1 (4%)	25	Transient Ischemic attack	0	0	0
Trabectedin	1 (4%)	25	Respiratory Failure	0	0	0
Trabectedin	1 (4%)	25	Febrile Neutropenia	1	0	0
Trabectedin	1 (4%)	25	Ulcerative Esophagitis	1	0	0

Non - Serious adverse event details and values

System organ class*: Blood/Bone Marrow, Gastrointestinal, Metabolic/Laboratory, Constitutional Symptoms

Event term*: Neutropenia, Leukopenia, Febrile neutropenia, Thrombocytopenia, Anemia, Vomiting, Nausea, Diarrhea, Fatigue, ALT/AST increased

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number
Trabectedin	19 (76%)	25	Leukopenia: Grade 1: 3(12%) Grade 2: 10 (40%) Grade 3: 6 (24%) Grade 4: 0
Trabectedin	18 (72%)	25	Neutropenia: Grade 1: 1 (4%) Grade 2: 6 (24%) Grade 3: 9 (36%) Grade 4: 2 (8%)
Trabectedin	3 (12%)	25	Febrile Neutropenia: Grade 1: 0 Grade 2: 0 Grade 3: 2 (8%) Grade 4: 1 (4%)
Trabectedin	9 (36%)	25	Thrombocytopenia: Grade 1: 4 (16%) Grade 2: 2 (8%) Grade 3: 1 (4%) Grade 4: 2 (8%)
Trabectedin	22 (88%)	25	Anemia: Grade 1: 12 (48%) Grade 2: 8 (32%) Grade 3: 2 (8%) Grade 4: 0
Trabectedin	8 (32%)	25	Vomiting: Grade 1: 7 (28%) Grade 2: 1 (4%) Grade 3: 0 Grade 4: 0
Trabectedin	9 (36%)	25	Nausea: Grade 1: 4 (16%) Grade 2: 5 (20%) Grade 3: 0 Grade 4: 0
Trabectedin	1 (4%)	25	Diarrhea: Grade 1: 1 (4%) Grade 2: 0 Grade 3: 0 Grade 4: 0
Trabectedin	12 (48%)	25	Fatigue: Grade 1: 5 (20%) Grade 2: 3 (12%) Grade 3: 4 (16%) Grade 4: 0

Trabectedin	18/21 (72%/84%)	25	AST/ALT Increased: Grade 1: 15/13 (60%/52%) Grade 2: 1/7 (4%/28%) Grade 3: 2/1 (8%/4%) Grade 4: 0/0
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? No

Date	Amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? No

If Yes, Interruption date

Interruption description

Limitations and caveats

None reported

Online references

Cancer Chemother Pharmacol (2016) 77: 477-484

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