Clinical trial results: *Studio randomizzato di fase II di chemioterapia ± metformina nel carcinoma del pancreas metastatico*

Summary

EudraCT number*	2010-020979-23
Trial protocol	PACT-17
Global end of trial date*	30Apr2015

Trial information

Trial identification	
Sponsor protocol code*	PACT-17
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01167738
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*	Feb 2014
Is this the analysis of the primary completion data?*	Yes
Global end of trial reached?*	Yes
Global end of trial date*	30Apr2015
Was the trial ended prematurely?	No

General information about the trial

Main objective of the trial*: To assess the therapeutic activity of chemotherapy comprising cisplatin, epirubicin hydrochloride, capecitabine, and gemcitabine hydrochloride with versus without metformin hydrochloride in terms of 6-month progression-free survival in patients with metastatic pancreatic cancer

Actual start date of recruitment*	10Aug2010
Long term follow-up planned*	Yes
If Yes, rationale:	Safety **Efficacy** Ethical reason Regulatory reason Scientific research
Duration	Years
Independent data monitoring committee (IDMC) involvement?*	Yes
Protection of trial subjects*:	Yes
Background therapy:	PEXG (Cisplatin, Epirubicin, Capecitabine, Gemcitabine)
Evidence for comparator:	

Population of trial subjects

Subjects enrolled per country

Country:	Italy
Planned number of subjects	82
Actual Number of subjects enrolled*	60
Worldwide total number of subjects	0
EEA total number of subjects	60 (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)*	33
From 65 to 84 years*	27
85 years and over*	0

Subject disposition

Recruitment details:

Enrollment from 10Aug2010 to 31Oct2013 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 pancreatic adenocarcinoma
- Metastatic (stage IV) disease
- Measurable disease
- No symptomatic brain metastases
- Karnofsky performance status 60-100%
- Not pregnant or nursing
- Adequate bone marrow, liver and kidney function
- No previous or concurrent malignancies at other sites except for surgically cured carcinoma in-situ of the cervix, basal cell or squamous cell carcinoma of the skin, or other neoplasms without evidence of disease within the past 5 years
- No multiple severe diseases which would compromise safety (i.e., cardiac failure, previous myocardial infarction within the past 4 months, cardiac arrhythmia, or history of psychiatric disabilities)
- No alcohol abuse
- No prior chemotherapy or metformin
- No other concurrent experimental drugs

Period 1	
Period title*	*Overall Trial*
Is this the baseline period?	No
Allocation method*	Randomised - controlled
Blinding used*	Not blinded

Arms	
Arm title*	**ARM A – PEXG+Metformin**
Arm description:	**PEXG regimen + metformin** *cisplatin and epirubicin at 30 mg/mq on days 1 and 15, capecitabine at 1250 mg/mq days 1-28, gemcitabine at 800 mg/mq on days 1 and 15, Metformin at 2 g days 1-28*
Arm type*	**Experimental**
Investigational medicinal product name*	**METFORMIN**
Investigational medicinal product code	
Other name	**GLUCOPHAGE**
Pharmaceutical forms*	**TABLETS**
Routes of administration*	**ORAL**
Dosage and administration details*	2 g day 1-28 every 4 weeks
Investigational medicinal product name*	**CISPLATIN**
Investigational medicinal product code	
Other name	

Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	30 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**EPIRUBICIN**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	30 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**GEMCITABINE**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	800 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**CAPECITABINE**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**TABLETS**
Routes of administration*	**ORAL**
Dosage and administration details*	1250 mg/mq days 1-28 every 4 weeks

Arm title*	**ARM B – PEXG**
Arm description:	**PEXG regimen + metformin** *cisplatin and epirubicin at 30 mg/mq on days 1 and 15, capecitabine at 1250 mg/mq days 1-28, gemcitabine at 800 mg/mq on days 1 and 15, Metformin at 2 g days 1-28*
Arm type*	**Active comparator**
Investigational medicinal product name*	**CISPLATIN**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	30 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**EPIRUBICIN**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	30 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**GEMCITABINE**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**VIALS**
Routes of administration*	**INTRAVENOUS**
Dosage and administration details*	800 mg/mq on days 1 and 15 every 4 weeks
Investigational medicinal product name*	**CAPECITABINE**
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	**TABLETS**

Routes of administration*	**ORAL**
Dosage and administration details*	1250 mg/mq days 1-28 every 4 weeks

Number of subjects in period	**ARM A – PEXG+Metformin**	**ARM B – PEXG**
Started*	31	29
Completed*	17	12
Subject non-completion reason (if applicable)	consent withdrawn	
AE, non fatal		
AE, fatal	1	0
Consent withdrawn by subject	1	0
Lack of efficacy	14	17
Lost to follow up	0	0
Physician decision	0	1
Pregnancy	0	0
Protocol Deviation		
Other		

Baseline characteristics

Reporting groups* Overall cohort	
Reporting group title*	PEXG+Metformin vs PEXG
Number of subjects at the baseline*	31 patients vs 29 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*	*ARM A: PEXG+Metformin*
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Patient assigned to ARM A (PEXG+Metformin) treatment who followed the study protocol without significant violations*
Number of subjects in subjects analysis set*	*31*

Subject analysis set title*	*PEXG*
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Patient assigned to ARM B (PEXG) treatment who followed the study protocol without significant violations*
Number of subjects in subjects analysis set*	*29*

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 63.5 years	full range (min-max) 42 – 75 years

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	Gender	Count	Female: 14 (ARM A), 16 (ARM B) Male: 17 (ARM A), 13 (ARM B)

Study specific characteristics

	Characteristic title*	Units *	Categories*	Number of subject for each categories
Study specific categorical	Karnofsky Performance status	count	70-80, 90-100	ARM A: 70-80 (11), 90-100 (20) ARM B: 70-80 (9), 90-100 (20)
Study specific categorical	Primary tumor location	count	Head, Body-Tail	ARM A: Head (14), Body-Tail (17) ARM B: Head (17), Body-Tail (12)
Study specific categorical	Diabetes at diagnosis	count	Present, Absent	ARM A: Present (23), Absent (8) ARM B: Present (22) Absent (7)
Study specific categorical				
Study specific categorical				

End points

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

Subject analysis set title*	ARM A: PEXG+Metformin
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 *	31

Subject analysis set title*	ARM B: PEXG
Subject analysis set type*	Per protocol
Subject analysis set description*	Patient assigned to ARM B (PEXG) treatment who followed the study protocol without significant violations
Number of subject in subject analysis set *	29

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 randomization 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 randomization 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

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*	PEXG+Metfomin	PEXG	
Period	Study Treatment Period	Study Treatment Period	
Arms	ARM A	ARM B	
subject analysis sets	Per protocol analysis sets for ARM A and ARM B	Per protocol analysis sets for ARM A and ARM B	

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: 10Aug2010
Last recruitment date: 10Jan2014
Study closure: 30Apr2015

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*	4.0.3

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*	60 (31 in arm A + 29 in arm B)
Subjects affected by non -SAE*	
Total number of deaths (all causes)*	
Total number of deaths resulting from adverse event*	

Serious adverse event details and values

System organ class*:

Event term*:

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

Non - Serious adverse event details and values

System organ class*:

Event term*:

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? yes

Date	Amendment
19Apr2013	Amen. # 1 (Administrative change)

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

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