Clinical trial results:
PHARMACOGENETIQUE DE LA GEMCITABINE : ETUDE DE L'IMPACT DU POLYMORPHISME GENETIQUE DE LA CYTIDINE DEAMINASE (CDA) SUR LA TOXICITE ET L'EFFICACITE THERAPEUTIQUE DANS LES ADENOCARCINOMES PANCREATIQUES RESEQUES

Summary

EudraCT number	2010-022987-11
Trial protocol	FR
Global end of trial date	15 September 2016

Results information

Result version number	v1 (current)
This version publication date	08 April 2022
First version publication date	08 April 2022

Trial information

Trial identification

Sponsor protocol code	FFCD 1004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01416662
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fédération Francophone de Cancérologie Digestive (FFCD)
Sponsor organisation address	7 Bd Jeanne d'Arc, Dijon, France, 21000
Public contact	Karine Le Malicot Head of Biostatistics, Fédération Francophone de Cancérologie Digestive (FFCD), karine.le-malicot@u-bourgogne.fr
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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	15 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2015
Global end of trial reached?	Yes
Global end of trial date	15 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluer la capacité du CDA à prédire la survenue d'une toxicité hématologique sévère (grade 3-4), précoce (lors des 2 premiers cycles), induite par la gemcitabine.

Protection of trial subjects:

The study was done in accordance with the Declaration of Helsinki (amended 2000) and the International Conference on Harmonization of Technical Requirements of Pharmaceuticals for Human Use (ICH) Note for Guidance on Good Clinical Practice and approved by the appropriate Ethics Committees.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2011
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	France: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	52
From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between July 2011 and June 2013, 120patients were enrolled in the trial by 31centers in France.

Pre-assignment

Screening details:

Before enrollement, standard examinations (biological, clinical, ECG) were done. In terms of imaging, abdominal and thoracic computed tomography
scan or MRI were also done.

Period 1

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

Arms

Arm title	Gemcitabin Arm

Arm description:

Adjuvant gemcitabine-monotherapy as follows: 30-minutes IV-infusion of 1000 mg/m2 every week for 3 consecutive weeks followed by one week off for 6 courses

Arm type	Experimental
Investigational medicinal product name	Gemcitabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Adjuvant gemcitabine-monotherapy as follows: 30-minutes IV-infusion of 1000 mg/m2 every week for 3 consecutive weeks followed by one week off for 6 courses

Number of subjects in period 1	Gemcitabin Arm
Started	120
Evaluable patients	109
Completed	109
Not completed	11
No matching reasons found	1
No CDA determination	10

Baseline characteristics

Reporting groups

Reporting group title	Enrolled patients

Reporting group description: -

Reporting group values	Enrolled patients	Total	
Number of subjects	120	120	
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)	52	52	
From 65-84 years	68	68	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	65.85		
standard deviation	± 10.05	-	
Gender categorical Units: Subjects			
Female	46	46	
Male	74	74	

Subject analysis sets

Subject analysis set title	Evaluable patients
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Is defined as all patients with a defined CDA phenotype-genotype who have received at least one administration of gemcitabine (regardless of dose).

Subject analysis set title	CDA <=1.3U/mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Patients treated with CDA <1.3U/mg

Subject analysis set title	CDA >1.3U/mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Patients treated with CDA >1.3 U/mg

Reporting group values	Evaluable patients	CDA <=1.3U/mg	CDA >1.3U/mg
Number of subjects	109	5	104
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)	47	2	45
From 65-84 years	62	3	59
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	65.74		
standard deviation	± 10.2	±	±
Gender categorical Units: Subjects			
Female	41		
Male	68		

End points

End points reporting groups

Reporting group title	Gemcitabin Arm
Reporting group description:	
Adjuvant gemcitabine-monotherapy as follows: 30-minutes IV-infusion of 1000 mg/m2 every week for 3 consecutive weeks followed by one week off for 6 courses	
Subject analysis set title	Evaluable patients
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Is defined as all patients with a defined CDA phenotype-genotype who have received at least one administration of gemcitabine (regardless of dose).	

Subject analysis set title	CDA <=1.3U/mg
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients treated with CDA <1.3U/mg	

Subject analysis set title	CDA >1.3U/mg
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients treated with CDA >1.3 U/mg	

Primary: Capability of CDA to predict occurence of severe toxicities

End point title	Capability of CDA to predict occurence of severe toxicities[1]
End point description:	

End point type	Primary
End point timeframe:	
Within 2 months of treatment	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study is a single-arm study so no comparison with a another arm.

End point values	Evaluable patients	CDA <=1.3U/mg	CDA >1.3U/mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	104	109	
Units: Patients				
Severe hematological toxicity	1	24	25	
No severe hematological toxicity	4	80	84	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

Until the end of the follow-up or death (Whatever the cause)

End point values	Gemcitabin Arm			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: patients				
Death	55			
Alive	65			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs occurring in the course of the study, from the signature of the informed consent form and until 30 days after the last dose of the study drug were reported by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	NCi-CTC
Dictionary version	4.0

Reporting groups

Reporting group title	Safety population

Reporting group description:

All the patients treated with at least one dose of treatment

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 119 (11.76%)		
number of deaths (all causes)	55		
number of deaths resulting from adverse events	0		
Investigations			
Hepatic function abnormal			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Eventration			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Alteration of general conditions			

subjects affected / exposed	2 / 119 (1.68%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hyperthermia			
subjects affected / exposed	3 / 119 (2.52%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Members Oedema			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
pneumopathy			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary fibrosis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	119 / 119 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 119 (5.04%)		
occurrences (all)	6		
Hypertension			
subjects affected / exposed	7 / 119 (5.88%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	93 / 119 (78.15%)		
occurrences (all)	93		
Fever			
subjects affected / exposed	34 / 119 (28.57%)		
occurrences (all)	34		
Chills			
subjects affected / exposed	17 / 119 (14.29%)		
occurrences (all)	17		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	11 / 119 (9.24%)		
occurrences (all)	11		
Cough			
subjects affected / exposed	14 / 119 (11.76%)		
occurrences (all)	14		
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	77 / 119 (64.71%)		
occurrences (all)	77		
Aspartate aminotransferase increased			
subjects affected / exposed	73 / 119 (61.34%)		
occurrences (all)	73		
bilirubin increased			
subjects affected / exposed	17 / 119 (14.29%)		
occurrences (all)	17		
Creatinine renal clearance increased			
subjects affected / exposed	8 / 119 (6.72%)		
occurrences (all)	8		
White blood cell count decreased			
subjects affected / exposed	90 / 119 (75.63%)		
occurrences (all)	90		
Haemoglobin increased			
subjects affected / exposed	9 / 119 (7.56%)		
occurrences (all)	9		
Neutrophil count decreased			
subjects affected / exposed	94 / 119 (78.99%)		
occurrences (all)	94		
Platelet count decreased			
subjects affected / exposed	63 / 119 (52.94%)		
occurrences (all)	63		
Gamma-glutamyltransferase increased			
subjects affected / exposed	46 / 119 (38.66%)		
occurrences (all)	46		
Phosphatases alcalines increased			
subjects affected / exposed	37 / 119 (31.09%)		
occurrences (all)	37		
Weight decreased			
subjects affected / exposed	7 / 119 (5.88%)		
occurrences (all)	7		
Nervous system disorders			

Headaches			
subjects affected / exposed	11 / 119 (9.24%)		
occurrences (all)	11		
Neuropathy			
subjects affected / exposed	8 / 119 (6.72%)		
occurrences (all)	8		
Paresthesia			
subjects affected / exposed	7 / 119 (5.88%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	115 / 119 (96.64%)		
occurrences (all)	115		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	8 / 119 (6.72%)		
occurrences (all)	8		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	67 / 119 (56.30%)		
occurrences (all)	67		
Oral mucositis			
subjects affected / exposed	13 / 119 (10.92%)		
occurrences (all)	13		
Nausea			
subjects affected / exposed	67 / 119 (56.30%)		
occurrences (all)	67		
Vomiting			
subjects affected / exposed	34 / 119 (28.57%)		
occurrences (all)	34		
Constipation			
subjects affected / exposed	30 / 119 (25.21%)		
occurrences (all)	30		
Stomach pain			
subjects affected / exposed	9 / 119 (7.56%)		
occurrences (all)	9		
Abdominal pain			

subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all)	42 / 119 (35.29%) 42 6 / 119 (5.04%) 6 6 / 119 (5.04%) 6 7 / 119 (5.88%) 7		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 21 / 119 (17.65%) 21 6 / 119 (5.04%) 6 9 / 119 (7.56%) 9		
Renal and urinary disorders Hematuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all)	 13 / 119 (10.92%) 13 12 / 119 (10.08%) 12		
Musculoskeletal and connective tissue disorders Dorsalgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Arthralgia	 19 / 119 (15.97%) 19 11 / 119 (9.24%) 11		

subjects affected / exposed	6 / 119 (5.04%)		
occurrences (all)	6		
cramps			
subjects affected / exposed	11 / 119 (9.24%)		
occurrences (all)	11		
Infections and infestations			
Infection			
subjects affected / exposed	13 / 119 (10.92%)		
occurrences (all)	13		
Metabolism and nutrition disorders			
Dysgeusia			
subjects affected / exposed	8 / 119 (6.72%)		
occurrences (all)	8		
Hyperglycaemia			
subjects affected / exposed	25 / 119 (21.01%)		
occurrences (all)	25		
Hyperkalaemia			
subjects affected / exposed	18 / 119 (15.13%)		
occurrences (all)	18		
Hypernatraemia			
subjects affected / exposed	6 / 119 (5.04%)		
occurrences (all)	6		
Hypoalbuminaemia			
subjects affected / exposed	23 / 119 (19.33%)		
occurrences (all)	23		
Hypocalcaemia			
subjects affected / exposed	12 / 119 (10.08%)		
occurrences (all)	12		
Hypokalaemia			
subjects affected / exposed	13 / 119 (10.92%)		
occurrences (all)	13		
Hyponatraemia			
subjects affected / exposed	11 / 119 (9.24%)		
occurrences (all)	11		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/2630894