Clinical trial results:
A Phase II study of lapatanib and capecitabine in the treatment of metastatic pancreatic cancer

Summary

EudraCT number	2008-006907-22
Trial protocol	IE
Global end of trial date	11 August 2010

Results information

Result version number	v1 (current)
This version publication date	24 February 2025
First version publication date	04 February 2021

Trial information

Trial identification

Sponsor protocol code	08-39

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00962312
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	Innovation House, Old Finglas Road, Dublin 11, Ireland, D11 KXN4
Public contact	Anna Shevlin, Cancer Trials Ireland, +353 16677211, info@cancertrials.ie
Scientific contact	Anna Shevlin, Cancer Trials Ireland, +353 16677211, info@cancertrials.ie

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	22 November 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2010
Global end of trial reached?	Yes
Global end of trial date	11 August 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Capecitabine in combination with Lapatinib, in terms of overall survival, in the first line treatment of patients with metastatic Pancreatic cancer.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations SI 190 of 2004 as amend and European Directive 2001/20/EC. The study was approved by the HPRA and SJH/AMNCH Research Ethics Committee.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	07 July 2009
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	Ireland: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	5

From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled in May 2009. 9 patients were recruited in total. The last patient was recruited in April 2010.

Pre-assignment

Screening details:

The target population will be chemotherapy naïve patients with a histologically or cytologically confirmed adenocarcinoma of the pancreas with evidence of metastatic disease

Period 1

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

Arms

Arm title	Overall Trial

Arm description:

Chemotherapy naïve patients with a histologically or cytologically confirmed adenocarcinoma of the pancreas with evidence of metastatic disease who fulfill all the Inclusion Criteria and none of the Exclusion Criteria

Arm type	Experimental
Investigational medicinal product name	Lapatinib
Investigational medicinal product code	GW572016
Other name	Tykerb,Tyverb
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients receive 1250mg/day lapatinib orally continuously for 21 days

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	Xeloda
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients will receive 1000mg/m2 capecitabine TWICE daily (morning and evening doses) orally on days 1-14 of the 21 day cycle

Number of subjects in period 1	Overall Trial
Started	9
Completed	9

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	9	9	
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)	5	5	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.06		
standard deviation	± 10.304	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	7	7	
Ethnic Origin Units: Subjects			
Caucasian	9	9	

End points

End points reporting groups

Reporting group title	Overall Trial

Reporting group description:

Chemotherapy naïve patients with a histologically or cytologically confirmed adenocarcinoma of the pancreas with evidence of metastatic disease who fulfill all the Inclusion Criteria and none of the Exclusion Criteria

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)[1]

End point description:

The study used the six-month survival as the Primary Endpoint. Patients who were still living six months after the last patient has been enrolled were to be censored for the analyses, using the number of days between enrolment and the date of their last follow-up as their overall survival measurement. The first stage of the study was to recruit 12 patients and if at least 7 met the survival criteria, a further 20 patients were to be enrolled. 9 patients were recruited to the first stage and 7 of them did not meet the overall survival criteria. Recruitment to the first stage was stopped to further accrual as the study primary outcome survival measure could no longer be met. Survival Analysis was therefore not carried out due to small numbers.

End point type	Primary

End point timeframe:

Overall survival will be defined as the interval between the date of first dose of study drug and the date of death.

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: Patients who were still living six months after the last patient has been enrolled were to be censored for the analyses, using the number of days between enrolment and the date of last follow-up. 7 out of the 9 patients recruited to the first stage did not meet this survival criteria. Recruitment to the first stage was stopped to further accrual as the study primary outcome survival measure could no longer be met. Survival Analysis was therefore not carried out due to small numbers.

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	9[2]			
Units: Months				
median (inter-quartile range (Q1-Q3))	5 (3.9 to 5.9)			

Notes:

[2] - Survival Analysis not carried out due to small numbers

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Patients who were still living six months after the last patient has been enrolled were to be censored for the analyses, using the number of days between enrolment and the date of last follow-up.
9 patients were recruited to the first stage and 7 of them did not meet the survival criteria. Recruitment to the first stage was stopped to further accrual as the study primary outcome survival measure could no longer be met. Survival Analysis was therefore not carried out due to small numbers.

End point type	Secondary

End point timeframe:

Measured in months (or fraction of months) from drug administration to disease progression

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	9[3]			
Units: Months				
median (inter-quartile range (Q1-Q3))	2.3 (1.5 to 3.0)			

Notes:

[3] - Analysis not carried out due to small number of patients

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: May 2009 - May 2010 (one year)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0
Reporting groups	
Reporting group title	Study Population
Reporting group description: Patients with a histologically or cytologically confirmed adenocarcinoma of the pancreas with evidence of metastatic disease	

Serious adverse events	Study Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Hyponatramia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage Left Lung			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain Right Lower Quadrant			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Raised Liver Profile			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Embolism/Left DVT			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Jaundice			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal Insufficiency			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain Iliac Crest			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection (unknown origin)			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Study Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Vascular disorders			
Phlebitis - Right Leg			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	6		
Weight Loss			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		

Tiredness				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Ankle Oedema				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Nose Bleed				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Swollen Ankles				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Pain in L ear				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Pyrexia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Dry Lips				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Back Pain				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Pain in big Right Toe				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Flu like illness				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
General Malaise				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			

Sore Mouth subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Cardiac disorders Hypotension subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nervous system disorders Neuropathy subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	6 / 9 (66.67%) 10 5 / 9 (55.56%) 8 5 / 9 (55.56%) 9 6 / 9 (66.67%) 8 5 / 9 (55.56%) 6		
Hepatobiliary disorders			

Pelvic Ascites			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
High Bilirubin			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
High Alk Phosphate			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hand and Foot Syndrome			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Erythema Hand and Feet			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Itching			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bruise Right Toe			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
angular cheilitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Facial Acne			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rash arms and legs			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Renal and urinary disorders			

High GGT			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Jaundice			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Stinging when passing urine			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Endocrine disorders			
High Lactate Dehydrogenase			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain -Calf			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Staph Aureus Bacteraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Low Potassium			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Hypoglycaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Low Sodium			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Poor Appetite			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2008	Amendment to Protocol - Updated to Version 2.0, 12Nov2008. Protocol cover page administrative changes: - protocol authors section deleted from cover page of protocol - Chief Investigator Dr Ray McDermott is noted instead now as "Chief Investigator (clinical)" - Dr Robert O'Connor, NICB Dublin City University is noted instead now as "Chief Investigator (translational)". - Addition of Sub Investigator: Dr Rizwan Sheikh at AMNCH Hospital. - Administrative change to Protocol: Summary of Time and Events table (Appendix C) - footnotes had not matched up correctly in previous protocol version - now corrected.
09 October 2009	Protocol updated to V3.0 20Aug 2009. Below are details of the updates: -Revised protocol template format (following an update to internal ICORG SOPs). Additional protocol text clarifications per study Chief Investigator: - Clarification that total dosage of 2000mg/m2/day is administered as 2 doses of 1000mg/m2 (morning and evening doses). - Table included as Appendix from Xeloda SPC for calculating standard and reduced doses of Capecitabine according to BSA for starting dose of 1000mg/m2. - Clarification that GSK are no longer prohibiting certain gastic pH modifiers (H2 blockers and PPIs). - Lapatinib specific rash management guidelines attached as Appendix. - Sub-study serum specimen procurement processing and storage details attached as Appendix. - Clarification revision of inclusion criterion no. 1: "patients must have histological or cytologically confirmed adenocarcinoma of the pancreas with evidence of metastatic disease." [previous noted as: patients must have histologically or cytologically confirmed metastatic adenocarcinoma of the pancreas]. - Clarification revisions to Time and Events Table: removal of 6-weekly procedures column from Table and related text - not required as all procedures are listed in 3-weekly procedures column and text.

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.

If seven or more patients to be recruited in the first stage had a six month survival, a further 20 patients were planned to be recruited to the second stage. The specified study survival criterion was not met and the study was stopped prematurely.

Notes: