Clinical trial results:
Pharmacokinetics and metabolic activation of capecitabine when given concomitantly with oxaliplatin and the monoclonal antibody cetuximab

Summary

EudraCT number	2011-002921-23
Trial protocol	AT
Global end of trial date	27 March 2014

Results information

Result version number	v1 (current)
This version publication date	27 July 2016
First version publication date	27 July 2016

Trial information

Trial identification

Sponsor protocol code	AGMT-Capecet_PK

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01579357
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AGMT
Sponsor organisation address	Gentzgasse 60/20, Vienna, Austria, 1180
Public contact	Daniela Wolkersdorfer, AGMT, 0043 6626404411, d.wolkersdorfer@agmt.at
Scientific contact	Richard Greil, AGMT, 0043 5725525801, r.greil@salk.at

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	27 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this pharmacokinetic study is to exclude a possible influence of CETUX on the plasma disposition and metabolic activation of Capecitabine (CCB) and when this regimen is given combined with Oxaliplatin (OxPt).

Protection of trial subjects:

Pretreatment before Cetuximab and chemotherapie was recommended. No additional investigating products, anti-tumoural drugs or drugs interacting with the EGFreceptor were allowed. Hematopoietic growth factors such as G-CSF could be used to treat neutropenia but should not be used prophylactically. Safety was monitored by reporting of clinical adverse events.

Background therapy:

Capecitabine 1000mg/m² bid q7d week 1,2,4,5,7 and 8
Oxaliplatin 130mg/m² iv day 1 week 7

Evidence for comparator: -

Actual start date of recruitment	06 March 2012
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	Austria: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	15
From 65 to 84 years	13

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 06-Mar-2012 and 07-Jan-2014 28 patients were enrolled at two sites in Austria.

Pre-assignment

Screening details:

Patients with histologically confirmed K-ras wild-type adenocarcinoma of the colon or rectum without previous chemotherapy for metastatic disease were screened for this study. Subjects who did not complete the entire study due to withdrawal or discontinuation for any reason were replaced.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Capecitabine in weeks 1, 2, 4, 5, 7 and 8
Cetuximab in weeks 3 to 9
Oxaliplatin in week 7

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

Dosage and administration details:

Cetuximab 400mg/m² (loading dose) or 250mg/m² iv day 1 week 3 to 9

Arm title	Arm B

Arm description:

Capecitabine in weeks 1, 2, 4, 5, 7 and 8
Cetuximab in weeks 1, 8 and 9
Oxaliplatin in week 7

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

Dosage and administration details:

Cetuximab 400mg/m² (loading dose) or 250mg/m² iv day 1 week 1, 8 and 9

Number of subjects in period 1	Arm A	Arm B
Started	15	13
Completed	12	12
Not completed	3	1
Physician decision	1	-
Adverse event, non-fatal	2	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	28	28	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
From 65-84 years	13	13	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	12	12	
Male	16	16	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Capecitabine in weeks 1, 2, 4, 5, 7 and 8 Cetuximab in weeks 3 to 9 Oxaliplatin in week 7	
Reporting group title	Arm B
Reporting group description:	
Capecitabine in weeks 1, 2, 4, 5, 7 and 8 Cetuximab in weeks 1, 8 and 9 Oxaliplatin in week 7	

Primary: A metabolic activation of CCB modulated by co-administered CETUX

End point title	A metabolic activation of CCB modulated by co-administered CETUX[1]
End point description:	
The objective of this pharmacokinetic study is to exclude a possible influence of CETUX on the plasma disposition and metabolic activation of CCB and when this regimen is given combined with OxPt.	
End point type	Primary
End point timeframe:	
9 weeks of study treatment per patient	

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: No data available up to this date

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Patients				

Notes:

[2] - No data available up to this date

[3] - No data available up to this date

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All (serious) adverse events occurring during study treatment were collected until 28 days after the end of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic complication			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Performance status decreased			

subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	4 / 28 (14.29%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Infection				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)		
Blood and lymphatic system disorders			
NA	Additional description: No data available up to this date		
subjects affected / exposed	28 / 28 (100.00%)		
occurrences (all)	28		

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