Clinical trial results:
Phase I/II study of lenalidomide and Cetuximab in patients with advanced solid tumors

Summary

EudraCT number	2009-013423-31
Trial protocol	AT
Global end of trial date	26 September 2012

Results information

Result version number	v1 (current)
This version publication date	21 August 2020
First version publication date	21 August 2020

Trial information

Trial identification

Sponsor protocol code	TEXO0309

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Christoph-Probst-Platz 1, Innrain 52 A, Innsbruck, Austria, 6020
Public contact	Ao.Univ.Prof.Dr. Heinz-Helmut Zwierzina, University Hospital for Internal Medicine I, +43 (0)50 504-36145, heinz-helmut.zwierzina@tirol-kliniken.at
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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	26 September 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2012
Global end of trial reached?	Yes
Global end of trial date	26 September 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the maximum tolerated dose (MTD) of lenalidomide administered in combination with cetuximab in patients with solid tumors

Protection of trial subjects:

Good tolerability and efficacy of lenalidomide (Revlimid®) have been clearly shown in multiple myeloma and in 5q- syndrome (a certain subtype of myelodysplastic syndrome (MDS)). Based on these data, lenalidomide has been approved for clinical application in these disorders and represents a tool for first line therapy.Excellent tolerability and efficacy of cetuximab (Erbitux®) given alone or in combination with various chemotherapeutic drugs have been demonstrated in several phase III trials and have lead to approval of cetuximab for clinical use in various solid tumors. Therefore clinical data of lenalidomide as well as cetuximab monotherapy suggest that no severe unforeseeable side effects are to be expected in this clinical trial using the combination of the drugs.

Background therapy:

Recommended concomitant therapy
· Full supportive care is permitted when appropriate, including transfusions of blood and blood products, antibiotics, or antiemetics.
· The use of haematopoietic growth factors is permitted, however should not be routinely used as prophylaxis to avoid dose reductions or delays.
· Aspirin, warfarin, low-molecular weight heparin, or other anticoagulant therapy is permitted.

Prohibited concomitant therapy
o Palliative radiation therapy is not permitted

Evidence for comparator: -

Actual start date of recruitment	12 August 2010
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: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects will be screened within 28 days of study entry. Subjects meeting all inclusion criteria will be enrolled in cohorts of three subjects.

Pre-assignment

Screening details:

Subjects will be screened within 28 days of study entry.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lenalidomide group

Arm description:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on
Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1. Patients will be hospitalized up to 3 days after Day 1 of Cycle 1.

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1.

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:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on
Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1.

Number of subjects in period 1	Lenalidomide group
Started	1
Completed	1

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lenalidomide group

Arm description:

All study subjects in Phase 1 or Phase 2 who discontinue from the study for any reason other than withdrawal of consent, will enter the Follow-up Period that includes one follow-up visit 28 days after last dose.

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1.

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:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on
Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1.

Number of subjects in period 2	Lenalidomide group
Started	1
Completed	0
Not completed	1
Evidence of progrssive disease	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	1	1	
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)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	0	0	

End points

End points reporting groups

Reporting group title	Lenalidomide group

Reporting group description:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on
Days 1, 8, 15, and 22 of each 28-day cycle.
Prior to Phase 1 Cycle 1, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1. Patients will be hospitalized up to 3 days after Day 1 of Cycle 1.

Reporting group title	Lenalidomide group

Reporting group description:

All study subjects in Phase 1 or Phase 2 who discontinue from the study for any reason other than withdrawal of consent, will enter the Follow-up Period that includes one follow-up visit 28 days after last dose.

Primary: MTD of lenalidomide administered in combination with cetuximab

End point title	MTD of lenalidomide administered in combination with cetuximab[1]

End point description:

Subjects meeting all inclusion criteria will be enrolled in cohorts of three patients to receive a single, oral dose of lenalidomide administered on Days 1-28 and intravenous (IV) infusions of cetuximab (400 mg/m2 first infusion only, then 250 mg/m2 subsequently) administered on Days 1, 8, 15, and 22 of each 28-day cycle. Prior to combination therapy, there will be a 21 day lead in treatment period with lenalidomide monotherapy (Days -21 to -1). Combination treatment will start at Day 1.
Cycles will be repeated every 28 days. All subjects will continue on study drug until disease progression, unacceptable toxicity or treatment discontinuation for any other reason.
Initial dose of Lenalidomide is 15mg (Dose Level 1).

End point type	Primary

End point timeframe:

Day 1- day 28

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: As only one subject was included in this trial no statistical anlysis was performed.

End point values	Lenalidomide group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Milligramm				
number (not applicable)				
Dose Level 1	15			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12.08.2010- 26.09.2012	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	Lenalidomide group

Reporting group description: -

Serious adverse events	Lenalidomide group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Bleeding after liver biopsy			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urosepsis			
subjects affected / exposed	1 / 1 (100.00%)		
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	Lenalidomide group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Injury, poisoning and procedural complications			

Bleeding after liver biopsy subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1		
Renal and urinary disorders Urosepsis subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2009	Addition zusätzlicher Stärken von Lenalidomidkapseln (10 mg, 15 mg und 20 mg Kapseln) für eine Erleichterung des Patienten bei der Medikationseinahme. Adaption des EudraCT-Formulars, des Prüfplans und der Patienteninformation/ Patienteneinverständniserklärung, sowie Nachreichung der nötigen Unterlagen betreffend der zusätzlichen Prüfpräparate. Lenalidomid is now availaible as capsules in additional concentrations (10 mg, 15 mg und 20 mg Kapseln). All relevant documents have been adapted to this circumstance.
18 March 2010	Das Protokoll musste geändert werden, da in der Medizinischen Universität Innsbruck ein neues PET-CT-Scan System verwendet wird, welches kein Solo-PET mehr durchführt, sondern nur mehr in Kombination mit einem CT durchgeführt wird. Somit ist eine Änderung der Patientensicherheit gegeben. Solo-PET was replaced with PET-CT Scan System, only combined analysis of PET and CT are possible now.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported