Clinical trial results:
Phase II study of Everolimus in refractory testicular germ cell cancer.

Summary

EudraCT number	2011-001502-10
Trial protocol	SK
Global end of trial date	15 June 2015

Results information

Result version number	v1 (current)
This version publication date	04 September 2021
First version publication date	04 September 2021

Trial information

Trial identification

Sponsor protocol code	GCTSK002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01466231
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Národný onkologický ústav
Sponsor organisation address	Klenova 1, Bratislava, Slovakia, 83310
Public contact	Oddelenie klinického skúšania, Národný onkologický ústav, 00421 259378592, daniela.svetlovska@nou.sk
Scientific contact	Oddelenie klinického skúšania, Národný onkologický ústav,, 00421 259378592, daniela.svetlovska@nou.sk

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	29 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2015
Global end of trial reached?	Yes
Global end of trial date	15 June 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy (as measured by response rate) of Everolimus in patients with refractory germ cell tumors (GCTs).

Protection of trial subjects:

All the procedures performed in the study involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	28 November 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	Slovakia: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From 28.11.2011 to 3.3.2015, a total of 16 patients were screened into to the study. One patient did not meet study eligibility criteria, 15 patients were analysed.
As no objective response was observed in the first 15 patients enrolled to the study, the study was terminated prematurely.

Pre-assignment

Screening details:

Refractory testicular cancer patients.

Period 1

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

Blinding implementation details:

NA

Arms

Arm title	Everolimus

Arm description:

Non-randomized, open-label, single arm trial with everolimus given orally (10 mg per day).

Arm type	Experimental
Investigational medicinal product name	everolimus
Investigational medicinal product code	L01XE10
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The starting dose was 10 mg daily. One cycle of therapy consisted of 28 days. The dose was administered orally once daily at the same time every day, consistently either with or without food. The patients were monitored closely for toxicity. Intrapatient dose reduction to 5 mg/day was allowed depending on the type and severity of toxicity encountered.

Number of subjects in period 1	Everolimus
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)

Reporting group description:

Single arm trial with everolimus given orally (10 mg per day).

Reporting group values	Overall study (overall period)	Total	
Number of subjects	15	15	
Age categorical			
Male patients age 18 years or older were eligible.			
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)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Only male patients were enrolled.			
Units: Subjects			
Female	0	0	
Male	15	15	

Subject analysis sets

Subject analysis set title	Overall study (overall period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Single arm trial with everolimus given orally (10 mg per day).

Reporting group values	Overall study (overall period)		
Number of subjects	15		
Age categorical			
Male patients age 18 years or older were eligible.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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 65-84 years	0		
85 years and over	0		
Gender categorical			
Only male patients were enrolled.			
Units: Subjects			
Female	0		
Male	15		

End points

End points reporting groups

Reporting group title	Everolimus
Reporting group description:	
Non-randomized, open-label, single arm trial with everolimus given orally (10 mg per day).	
Subject analysis set title	Overall study (overall period)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Single arm trial with everolimus given orally (10 mg per day).	

Primary: Response rate

End point title	Response rate
End point description:	
None of the enrolled patients had partial or complete response to the study treatment.	
End point type	Primary
End point timeframe:	
Objective response rate is defined as sum of complete and partial responses. It is defined from start of the treatment until progression of disease or start of new anticancer treatment.	

End point values	Everolimus	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15[1]		
Units: number of subjects	0	0		

Notes:

[1] - No objective response was observed in first 15 patients, therefore study was terminated.

Statistical analyses

Statistical analysis title	descriptive statistics
Statistical analysis description:	
No objective response was observed in first 15 patients, therefore study wasterminated due to futility.	
Comparison groups	Everolimus v Overall study (overall period)
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 5
Method	Chi-squared

Notes:

[2] - 15 patients were analysed, subject in analysis 30 is number automatically doubling by the system

Secondary: Favourable response rate

End point title	Favourable response rate
End point description:	
Favorable response will be classified complete remission and/or partial response with normalized serum tumor markers in case they were elevated before treatment. All other responses are considered as unfavourable.	

None of the enrolled patients had partial or caomplete response to the study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment to the best response of the study treatment.

End point values	Everolimus	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: number of patients	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression- free survival

End point title	Progression- free survival

End point description:

End point type	Secondary

End point timeframe:

Progression-free survival (PFS) will be calculated from the beginning of the treatment until progression or death from disease-specific cause on intention-to-treat basis.

End point values	Everolimus	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: month				
number (confidence interval 95%)	1.7 (1.1 to 4.0)	1.7 (1.1 to 4.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum tumor markers response

End point title	Serum tumor markers response

End point description:

>90% decline of AFP and/or HCG had none the enrolled patients.

End point type	Secondary

End point timeframe:

From start of treatment until disease progression.

End point values	Everolimus	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: month	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from start of study treatment until 28 days after study treatment discontinuation.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	All subjects

Reporting group description:

Grade 3 and 4 non serious or any grade serious adverse events are reported. Subjects affected by all grades non serious adverse events are 12, by grade 3-4 non serious adverse events are 4 subjects, by any grade SAE 9 patients.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 15 (60.00%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain	Additional description: 1 patient experienced SAE tumor related pain.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracerebral hemorrhage	Additional description: 1 patient experienced SAE intracerebral hemorrhage.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disease progression	Additional description: 5 patient experienced SAE disease progression.		
subjects affected / exposed	5 / 15 (33.33%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 5		
Vascular disorders			
Thrombosis of vena jugularis	Additional description: 1 patient experienced SAE thrombosis of vena jugularis.		

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epileptic seizure	Additional description: 1 patient experienced SAE epileptic seizure.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis	Additional description: 1 patient experienced SAE pneumonitits.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia	Additional description: 1 patient experienced SAE anorexia.		
subjects affected / exposed	1 / 15 (6.67%)		
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	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)		
Investigations			
Platelet count decreased	Additional description: grade 3 non serious		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood bilirubin increased	Additional description: grade 3		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia	Additional description: grade 3 and 4		
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
General disorders and administration			

site conditions			
Fatigue	Additional description: grade 3		
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypertriglyceridaemia	Additional description: grade 3 non serious		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hyperlipidaemia	Additional description: grade 3 and 4		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Anorexia	Additional description: grade 3 non serious		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

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/26612480