Clinical trial results:
Phase II study of gemcitabine, carboplatin and VELIPARIB (ABT-888) in refractory testicular germ cell cancer.

Summary

EudraCT number	2016-000171-24
Trial protocol	SK
Global end of trial date	12 February 2021

Results information

Result version number	v2 (current)
This version publication date	04 September 2021
First version publication date	08 August 2021
Version creation reason	• Correction of full data set corr
Summary attachment (see zip file)	GCTSK004 summary (GCTSK004 summary.pdf)

Trial information

Trial identification

Sponsor protocol code	GCTSK004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02860819
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Národný onkologický ústav
Sponsor organisation address	Klenová 1, Bratislava, Slovakia, 83310
Public contact	Department of Clinical Trials, Národný onkologický ústav, +421 259378592, daniela.svetlovska@nou.sk
Scientific contact	Department of Clinical Trials, Národný onkologický ústav, +421 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	15 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2021
Global end of trial reached?	Yes
Global end of trial date	12 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy (as measured by 12-months progression-free survival) of gemcitabine, carboplatin and VELIPARIB (ABT-888) in patients with refractory germ cell tumors (GCTs).

Protection of trial subjects:

All the procedures performed in studies 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 Informed consent was obtained from all individual participants included in the study.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	01 August 2016
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:

Recruitment period lasted from 01/AUG/2016 to 18/JUN/2020 considering 15 evaluable patients enrolled. As primary objective was not reached in first 15 patients enrolled (Stage I), study was terminated and enrollment of another 28 patients (Stage II)) did not start.

Pre-assignment

Screening details:

The main inclusion criteria included multiple relapsed/refractory extracranial primary germ cell cancers (either seminoma or non-seminoma) pre-treated with cisplatin-based chemotherapy.

Total of 16 patients were screened and 15 of them were assigned to the treatment, 1 patient was screening failure as did not fulfill all criteria.

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

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	Gemcitabine, carboplatin and veliparib

Arm description:

Gemcitabine was administered intravenously at a dose of 800 mg/m2 on days 1 and 8 every 3 weeks; carboplatin at a target AUC of 4 on day 1 every 3 weeks; and veliparib at a dose of 250 mg b.i.d. throughout.

Arm type	Experimental
Investigational medicinal product name	gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A dose of 800 mg/m2 on days 1 and 8 every 3 weeks

Investigational medicinal product name	carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin AUC = 4, day 1, every 3 weeks

Investigational medicinal product name	veliparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Oral use

Dosage and administration details:

Veliparib 250mg bid day continuously

Number of subjects in period 1	Gemcitabine, carboplatin and veliparib
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Gemcitabine, carboplatin and veliparib

Reporting group description:

Gemcitabine was administered intravenously at a dose of 800 mg/m2 on days 1 and 8 every 3 weeks; carboplatin at a target AUC of 4 on day 1 every 3 weeks; and veliparib at a dose of 250 mg b.i.d. throughout.

Reporting group values	Gemcitabine, carboplatin and veliparib	Total	
Number of subjects	15	15	
Age categorical			
Adult men above 18 years old.			
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	
Adult men	0	0	
Adults	0	0	
Gender categorical			
Male subjects			
Units: Subjects			
Female	0	0	
Male	15	15	

Subject analysis sets

Subject analysis set title	Gemcitabine, carboplatin, veliparib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All 15 patients assigned to study treatment were analysed.

Reporting group values	Gemcitabine, carboplatin, veliparib		
Number of subjects	15		
Age categorical			
Adult men above 18 years old.			
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		
Adult men	0		
Adults	0		
Gender categorical			
Male subjects			
Units: Subjects			
Female	0		
Male	15		

End points

End points reporting groups

Reporting group title	Gemcitabine, carboplatin and veliparib

Reporting group description:

Gemcitabine was administered intravenously at a dose of 800 mg/m2 on days 1 and 8 every 3 weeks; carboplatin at a target AUC of 4 on day 1 every 3 weeks; and veliparib at a dose of 250 mg b.i.d. throughout.

Subject analysis set title	Gemcitabine, carboplatin, veliparib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All 15 patients assigned to study treatment were analysed.

Primary: 12-months progression-free survival rate

End point title	12-months progression-free survival rate

End point description:

Twelve-month PFS was achieved in 1 (6.7 %) patient.

End point type	Primary

End point timeframe:

12-month progression-free survival was defined as number of living patients without progression after 12 month of start of study treatment.

End point values	Gemcitabine, carboplatin and veliparib	Gemcitabine, carboplatin, veliparib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: number of subjects	1	1		

Statistical analyses

Statistical analysis title	descriptive statistics

Statistical analysis description:

If fewer than 8 patients were alive and progression-free at 12 months among the first 15 patients, the study would be terminated. If a 12-month PFS occurred in at least 8 patients, the study would continue with a second cohort of an additional 28 patients.

Comparison groups	Gemcitabine, carboplatin and veliparib v Gemcitabine, carboplatin, veliparib
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 5
Method	Chi-squared

Notes:

[1] - 15 patients were analysed; subject in analysis 30 is number, doubling automatically by the system

Secondary: Response rate

End point title	Response rate

End point description:

End point type	Secondary

End point timeframe:

Objective response rate is defined as sum of complete and partial responses. It is defined from start of the treatment until disease progression or start of new anticancer treatment or other reason.

End point values	Gemcitabine, carboplatin and veliparib			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: number of subjects	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Median overall survival

End point title	Median overall survival

End point description:

End point type	Secondary

End point timeframe:

Overall survival (OS) was calculated from the beginning of the treatment until death from any cause on intention-to-treat basis.

End point values	Gemcitabine, carboplatin and veliparib			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: month				
median (confidence interval 95%)	10.5 (8.9 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median progression-free survival

End point title	Median 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	Gemcitabine, carboplatin and veliparib			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: month				
median (confidence interval 95%)	3.1 (2.2 to 3.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting period starts from time patient provides informed consent to 28 day of the last study drug administration. In case investigator believes, that SAE is related to study drug, it should be reported also after 28 days of the last study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	All subjects

Reporting group description:

All AE for all grades were collected. We publish all SAE and most severe AE so grade 3/4.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
febrile neutropenia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
General disorders and administration site conditions			
death due to disease prigression			
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			
pneumothorax			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
sepsis			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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	15 / 15 (100.00%)		
Investigations			
neutropenia	Additional description: grade 3/4 neutropenia only		
subjects affected / exposed	11 / 15 (73.33%)		
occurrences (all)	11		
thrombocytopenia	Additional description: grade 3/4 only		
subjects affected / exposed	10 / 15 (66.67%)		
occurrences (all)	10		
Nervous system disorders			
epileptic seizure	Additional description: grade 4		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
syncope	Additional description: grade 3		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
anemia	Additional description: grade 3/4 anemia only		
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	5		
febrile neutropenia	Additional description: non serious was one, serious another one		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
pain after drainage	Additional description: grade 3		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
chest pain non-cardiac	Additional description: grade 3		

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
vomiting	Additional description: grade 3		
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Infections and infestations			
catheter related infection	Additional description: grade 3		
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? Yes

Date	Amendment
05 January 2018	Amendment protocol, version 2.0, 11.10.2017

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.

NA

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34052929