Clinical trial results:
A treatment strategy of the Use of 1st line Chemotherapy in Patients with Poor-Prognosis Disseminated Non-Seminomatous Germ Cell Tumors based on tumor marker decline: A Phase II Trial of paclitaxel, ifosfamid and cisplatin regimen

Summary

EudraCT number	2014-001270-33
Trial protocol	SK
Global end of trial date	01 June 2021

Results information

Result version number	v1 (current)
This version publication date	13 August 2022
First version publication date	13 August 2022

Trial information

Trial identification

Sponsor protocol code	GCTSK003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02414685
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Národný onkologický ústav
Sponsor organisation address	Klenova 1, Bratislava, Slovakia, 833 10
Public contact	Prof Michal Mego MD, DSc,, Národný onkologický ústav, 00421 259378108, michal.mego@nou.sk
Scientific contact	Prof Michal Mego MD, DSc,, Národný onkologický ústav, 00421 259378108, michal.mego@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	23 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2021
Global end of trial reached?	Yes
Global end of trial date	01 June 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy (defined as complete response rate) of TIP in the 1st line treatment of patients with poor prognosis NSGCT and an unfavorable decrease in the serum level of tumor markers after 1 cycle of the BEP regimen.

Protection of trial subjects:

All the procedures performed in 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 paricipants included in the study.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	14 August 2015
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From 18 November 2015 to 27 March 2020 , a total of 21 patients were screened into the study. One patient did not meet study eligibility criteria, 20 subjects were enrolled and receive study treatment.

Pre-assignment

Screening details:

Patients with Disseminated Nonseminomatous Germ Cell Tumors with a poor prognosis according to the International Germ Cell Cancer Collaboration Group classification and an unfavorable Serum Tumor Markerdecline after the first cycle of chemotherapy

Pre-assignment period milestones

Number of subjects started	20
Number of subjects completed	

Period 1

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

Arms

Arm title	TIP -Paclitaxel, Ifosfamid, Cisplatin

Arm description:

4 cycles of TIP regimen:
Taxol 250 mg/ m2 iv on day 1
Ifosfamid 1,2 g/ m2/ day iv x 5 days
Cisplatin 20 mg/ m2/ day iv x 5 days.
One cycle of therapy consists of 21 days.

Arm type	Experimental
Investigational medicinal product name	Ifosfamid
Investigational medicinal product code	SUB08125MIG
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 mg/m2 on days 1-5, every 21 days, totally for four cycles.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	SUB09583MIG
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

paclitaxel 250 mg/m2 on day 1, every 21 days, totally for four cycles.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	SUB07483MIG
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
cisplatin 20 mg/m2 on days 1-5, every 21 days, totally for four cycles.

Number of subjects in period 1	TIP -Paclitaxel, Ifosfamid, Cisplatin
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title	Overall Study (overall period)

Reporting group description:

an open-labeled, nonrandomized, single arm trial with .the treatment regimen consisted of paclitaxel 250 mg/m2 on day 1, ifosfamide 1200 mg/m2 on days 1-5, and cisplatin 20 mg/m2 on days 1-5, totally for four cycles

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	20	20	
Age categorical			
Male subjects 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)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Adults from 18 years	0	0	
Gender categorical			
Male subjects only			
Units: Subjects			
Male	20	20	

Subject analysis sets

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

Subject analysis set description:

An open-labeled, non-randomized, single arm trial with the treatment regimen consisted of paclitaxel 250 mg/m2 on day 1, ifosfamide 1200 mg/m2 on days 1-5, and cisplatin 20 mg/m2 on days 1-5, given intravenously every 21 days, totally for four cycles

Reporting group values	Overall study (overall period)		
Number of subjects	20		
Age categorical			
Male subjects 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)	20		
From 65-84 years	0		
85 years and over	0		
Adults from 18 years	0		
Gender categorical			
Male subjects only			
Units: Subjects			
Male	20		

End points

End points reporting groups

Reporting group title	TIP -Paclitaxel, Ifosfamid, Cisplatin

Reporting group description:

4 cycles of TIP regimen:
Taxol 250 mg/ m2 iv on day 1
Ifosfamid 1,2 g/ m2/ day iv x 5 days
Cisplatin 20 mg/ m2/ day iv x 5 days.
One cycle of therapy consists of 21 days.

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

Subject analysis set description:

An open-labeled, non-randomized, single arm trial with the treatment regimen consisted of paclitaxel 250 mg/m2 on day 1, ifosfamide 1200 mg/m2 on days 1-5, and cisplatin 20 mg/m2 on days 1-5, given intravenously every 21 days, totally for four cycles

Primary: Complete Response Rate

End point title	Complete Response Rate

End point description:

Complete response to chemotherapy alone is defined as disappearance of all clinical, radiographic, and biochemical evidence of disease for at least 4 weeks; this includes patients in
whom surgical resection of residuum yields necrotic debris, fibrosis, or mature teratoma but no evidence of viable malignant tumor.
Complete response to chemotherapy plus surgery is defined as complete excision of all masses, at least one of which contained viable tumor other than mature teratoma.

End point type	Primary

End point timeframe:

Complete Response Rate was calculated from the start of the treatment until progression or death.

End point values	TIP -Paclitaxel, Ifosfamid, Cisplatin	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20[1]	20[2]		
Units: number of subjects	4	4		

Notes:

[1] - A CR was achieved in four subjects, therefore, the study was terminated in the first stage.

[2] - A CR was achieved in four subjects, therefore, the study was terminated in the first stage.

Statistical analyses

Statistical analysis title	descriptive statistics
Comparison groups	TIP -Paclitaxel, Ifosfamid, Cisplatin v Overall study (overall period)
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	< 5
Method	Chi-squared

Secondary: Toxicity grade 3/4

End point title	Toxicity grade 3/4

End point description:

Adverse events will be assessed before each cycle of chemotherapy according to the NCI Common Toxicity Criteria (CTC) version 4.1.

End point type	Secondary

End point timeframe:

Adverse events will be assessed from the start of the first chemotherapy until 28 days of completion of last chemotherapy.

End point values	TIP -Paclitaxel, Ifosfamid, Cisplatin	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20[3]	20		
Units: number of subjects	9	9		

Notes:

[3] - any grade 3/4 txity had 9 subjects, 47,4 %

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate

End point title	Response rate

End point description:

Objective response rate is defined as sum of complete and partial responses.

End point type	Secondary

End point timeframe:

From the beginning of the treatment until progression or death or start of new anticancer treatment.

End point values	TIP -Paclitaxel, Ifosfamid, Cisplatin	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20[4]	20		
Units: number of patients	15	15		

Notes:

[4] - A favorable response rate (CR or PR with negative tumor markers) was observed in 15 subjects.

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:

From the beginning of the treatment until progression or death.

End point values	TIP -Paclitaxel, Ifosfamid, Cisplatin	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20	20		
Units: month				
median (confidence interval 95%)	18.4 (5.5 to 21.9)	18.4 (5.5 to 21.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

OS was calculated from the date of starting the treatment with TIP to the date of death or last follow-up.

End point values	TIP -Paclitaxel, Ifosfamid, Cisplatin	Overall study (overall period)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20	20		
Units: month				
median (confidence interval 95%)	28.8 (19.5 to 28.8)	28.8 (19.5 to 28.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events wee reccorded from start of study tretment until 28 days after last chemotherapy administration.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.1

Reporting groups

Reporting group title	all subjects

Reporting group description:

Grade 3 and 4 non serious or any grade serious adverse events are reported.

Serious adverse events	all subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: 1 subject experiences Febrile neutropenia, Grade 3, related to study treatment.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever	Additional description: 1 subject experienced and was hospitalised for Fever, grade 1, related to study treatment.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: 1 subject experienced Sepsis,Gr. 4,not related to study drug.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 20 (45.00%)		
Vascular disorders			
Syncope	Additional description: 2 subjects experienced Syncope, Gr.3		
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Thrombosis	Additional description: 1 subject experienced Thrombosis, Gr.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Paresthesia	Additional description: 1 subject experienced Paresthesia, Gr.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia	Additional description: 6 subjects experienced Neutropenia, Gr.3 or Gr. 4.		
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	6		
Thrombocytopenia	Additional description: 2 subjects experienced Thrombocytopenia, Gr.3. or Gr.4.		
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Anaemia	Additional description: 4 subjects experienced Anaemia, Gr.3.		
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Febrile neutropenia	Additional description: 2 subjects experienced Febrile neutropenia, Gr.3. (one was SAE, second one only AE)		
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue	Additional description: 1 subject experienced Fatigue, Gr.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Tumor duodenal fistula	Additional description: 1 subject experienced Tumor duodenal fistula, Gr.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Insult on the finger of the hand	Additional description: 1 subject experienced Insult on the finger of the hand, Gr.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			
Infection NOS	Additional description: 1 subject experienced infection not otherwise specified, Ge.3.		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal abscess	Additional description: 1 subject experienced Abdominal abscess, Gr.3		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2019	Protocol ver.2.0 dated 15May2019.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported