



## 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<br>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,<br>+421 259378592, daniela.svetlovska@nou.sk |
| Scientific contact           | Department of Clinical Trials, Národný onkologický ústav,<br>+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/m<sup>2</sup> 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/m<sup>2</sup> 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

| <b>Number of subjects in period 1</b> | Gemcitabine,<br>carboplatin and<br>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/m<sup>2</sup> 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:<br>Gemcitabine was administered intravenously at a dose of 800 mg/m <sup>2</sup> 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:<br>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:<br>Twelve-month PFS was achieved in 1 (6.7 %) patient.   |  |
| End point type  | Primary                                  |
| End point timeframe:<br>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:<br>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 <sup>[1]</sup>   |
| 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. |               |

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | 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. |                         |

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | 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. |                                  |

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | 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 prgression                      |                 |  |  |
| 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 %

| <b>Non-serious adverse events</b>                     | 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:

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### 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:

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### Online references

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