



## Clinical trial results:

### Nivolumab, ipilimumab and radiation in combination with influenza vaccine in patients with pancreatic cancer.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2021-003931-27  |
| Trial protocol           | DK              |
| Global end of trial date | 19 October 2023 |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 25 September 2024 |
| First version publication date | 25 September 2024 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | GI2118 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05116917 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Department of Oncology, Herlev & Gentofte Hospital   |
| Sponsor organisation address | Borgmester Ib Juuls Vej 1, Herlev, Denmark, 2730   |
| Public contact               | Principal Investigator Inna Chen, Department of Oncology, Herlev & Gentofte Hospital, +45 38682898, inna.chen@regionh.dk |
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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                       | 09 April 2024   |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 19 October 2023 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 19 October 2023 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of nivolumab, ipilimumab and radiation in combination with influenza vaccine in terms of objective response rate (ORR).

Protection of trial subjects:

Patients that signed informed consent and fulfilling eligibility criteria were included. Continued monitoring of standard safety parameters during treatment.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 05 November 2021 |
| 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 | Denmark: 19 |
| Worldwide total number of subjects   | 19          |
| EEA total number of subjects         | 19          |

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)                      | 10 |
| From 65 to 84 years                       | 9  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The trial was open for recruitment of patients from November 2021 to May 2023. All patients are recruited at a single site: Copenhagen University Hospital - Herlev and Gentofte in Denmark. Trial is prematurely ended due to lack of efficacy at preplanned interim analysis.

### Pre-assignment

Screening details:

Eligible patients were  $\geq 18$  years with advanced pancreatic cancer with PD after at least one line of treatment, ECOG PS 0-1, adequate organ and hematologic function.

### Period 1

|                              |                                      |
|------------------------------|--------------------------------------|
| Period 1 title               | INFLUENCE Treatment (overall period) |
| Is this the baseline period? | Yes                                  |
| Allocation method            | Not applicable                       |
| Blinding used                | Not blinded                          |

### Arms

|           |                                       |
|-----------|---------------------------------------|
| Arm title | Nivo/Ipi + SBRT and influenza vaccine |
|-----------|---------------------------------------|

Arm description:

SBRT of 15 Gy will be given on day 1 of the first cycle. Nivolumab 3 mg/kg (up to 240 mg maximum) will be given on day 1 ( $\pm 3$  days) of each 14-day treatment cycle until the progression of disease or maximum of 48 weeks, discontinuation due to toxicity, withdrawal of consent. Ipilimumab 1 mg/kg will be given on day 1 cycle 1 ( $\pm 3$  days) and once more after 6 weeks.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Nivolumab                             |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Nivolumab 3 mg/kg (up to 240 mg maximum) given on day 1 ( $\pm 3$  days) of each 14-day treatment cycle until the progression of disease or maximum of 48 weeks, discontinuation due to toxicity, withdrawal of consent.

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Ipilimumab                            |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Ipilimumab 1 mg/kg given on day 1 cycle 1 ( $\pm 3$  days) and once more after 6 weeks.

|  |   |
|--|---|
| Investigational medicinal product name | Seasonal quadrivalent influenza vaccine         |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Suspension for injection in pre-filled injector |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

Seasonal influenza vaccine is given IM or via PharmaJet Stratis Needle-Free Injection System, 0.5 mL per dose as a single on day 1 cycle 1

| <b>Number of subjects in period 1</b> | Nivo/Ipi + SBRT and influenza vaccine |
|---------------------------------------|---------------------------------------|
| Started                               | 19                                    |
| Completed                             | 17                                    |
| Not completed                         | 2                                     |
| Adverse event, serious fatal          | 1                                     |
| Adverse event, non-fatal              | 1                                     |

## Baseline characteristics

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Nivo/Ipi + SBRT and influenza vaccine |
|-----------------------|---------------------------------------|

Reporting group description:

SBRT of 15 Gy will be given on day 1 of the first cycle. Nivolumab 3 mg/kg (up to 240 mg maximum) will be given on day 1 ( $\pm$  3 days) of each 14-day treatment cycle until the progression of disease or maximum of 48 weeks, discontinuation due to toxicity, withdrawal of consent. Ipilimumab 1 mg/kg will be given on day 1 cycle 1 ( $\pm$  3 days) and once more after 6 weeks.

| Reporting group values                               | Nivo/Ipi + SBRT and influenza vaccine | Total |  |
|--|---------------------------------------|-------|--|
| Number of subjects                                   | 19                                    | 19    |  |
| Age categorical                                      |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| Adults (18-64 years)                                 | 10                                    | 10    |  |
| From 65-84 years                                     | 9                                     | 9     |  |
| 85 years and over                                    | 0                                     | 0     |  |
| Age continuous                                       |                                       |       |  |
| Units: years   |                                       |       |  |
| median   | 62                                    |       |  |
| full range (min-max)                                 | 35 to 76                              | -     |  |
| Gender categorical                                   |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| Female   | 8                                     | 8     |  |
| Male   | 11                                    | 11    |  |
| ECOG Performance status                              |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| PS 0   | 12                                    | 12    |  |
| PS 1   | 7                                     | 7     |  |
| Prior surgery of primary tumor                       |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| Yes  | 6                                     | 6     |  |
| No   | 13                                    | 13    |  |
| Number of metastatic sites                           |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| =1   | 6                                     | 6     |  |
| >=2  | 13                                    | 13    |  |
| Number of prior treatment lines for advanced disease |                                       |       |  |
| Units: Subjects                                      |                                       |       |  |
| =1   | 2                                     | 2     |  |
| >=2  | 17                                    | 17    |  |

## End points

### End points reporting groups

|   |                                       |
|---|---------------------------------------|
| Reporting group title   | Nivo/Ipi + SBRT and influenza vaccine |
| Reporting group description:<br>SBRT of 15 Gy will be given on day 1 of the first cycle. Nivolumab 3 mg/kg (up to 240 mg maximum) will be given on day 1 ( $\pm$ 3 days) of each 14-day treatment cycle until the progression of disease or maximum of 48 weeks, discontinuation due to toxicity, withdrawal of consent. Ipilimumab 1 mg/kg will be given on day 1 cycle 1 ( $\pm$ 3 days) and once more after 6 weeks. |                                       |

### Primary: Objective Response Rate

|  |  |
|--|--|
| End point title  | Objective Response Rate <sup>[1]</sup> |
| End point description:<br>The primary endpoint of ORR, according to investigator assessment, is defined as the number (%) of subjects with at least one visit response of confirmed CR or PR |  |
| End point type   | Primary                                |
| End point timeframe:<br>tumor response was assessed by CT-scan every 8 week during treatment for the individual patients   |  |

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: Single arm, not to be compared to historical data.

Predictive probability based on the first 17 patients with possibility of 13 further observations was at only 0.7% (10 % was defined cut-off for continuation). Therefore, inclusion of patients was discontinued at the time.

| End point values            | Nivo/Ipi + SBRT and influenza vaccine |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 19 <sup>[2]</sup>                     |  |  |  |
| Units: percent              |                                       |  |  |  |
| number (not applicable)     | 0                                     |  |  |  |

Notes:

[2] - At least one follow-up imaging (n=13)

No post-baseline imaging (n=6)

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AE were collected from initiation of study treatment until 100 days after discontinuation of dosing or until starting a new anti-neoplastic therapy (whichever occurred first)

Adverse event reporting additional description:

All serious AE are reported. Non serious adverse event are reported if events were assessed with causal relationship to study treatment only.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |           |
|-----------------|-----------|
| Dictionary name | NCI-CTCAE |
|-----------------|-----------|

|                    |   |
|--------------------|---|
| Dictionary version | 5 |
|--------------------|---|

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Nivo/Ipi + SBRT and influenza vaccine |
|-----------------------|---------------------------------------|

Reporting group description:

SBRT of 15 Gy will be given on day 1 of the first cycle. Nivolumab 3 mg/kg (up to 240 mg maximum) will be given on day 1 ( $\pm$  3 days) of each 14-day treatment cycle until the progression of disease or maximum of 48 weeks, discontinuation due to toxicity, withdrawal of consent. Ipilimumab 1 mg/kg will be given on day 1 cycle 1 ( $\pm$  3 days) and once more after 6 weeks.

| Serious adverse events                            | Nivo/Ipi + SBRT and influenza vaccine |  |  |
|---|---------------------------------------|--|--|
| Total subjects affected by serious adverse events |                                       |  |  |
| subjects affected / exposed                       | 9 / 19 (47.37%)                       |  |  |
| number of deaths (all causes)                     | 19                                    |  |  |
| number of deaths resulting from adverse events    | 1                                     |  |  |
| Investigations                                    |                                       |  |  |
| Blood creatine increased                          |                                       |  |  |
| subjects affected / exposed                       | 1 / 19 (5.26%)                        |  |  |
| occurrences causally related to treatment / all   | 1 / 1                                 |  |  |
| deaths causally related to treatment / all        | 0 / 0                                 |  |  |
| Nervous system disorders                          |                                       |  |  |
| Seizure   |                                       |  |  |
| subjects affected / exposed                       | 1 / 19 (5.26%)                        |  |  |
| occurrences causally related to treatment / all   | 0 / 1                                 |  |  |
| deaths causally related to treatment / all        | 0 / 0                                 |  |  |
| Hepatobiliary disorders                           |                                       |  |  |
| Hepatitis   |                                       |  |  |

|   |  |  |  |
|---|--|--|--|
| subjects affected / exposed                     | 1 / 19 (5.26%)                                 |  |  |
| occurrences causally related to treatment / all | 0 / 1  |  |  |
| deaths causally related to treatment / all      | 0 / 0  |  |  |
| Hepatic encephalopathy                          |  |  |  |
| subjects affected / exposed                     | 1 / 19 (5.26%)                                 |  |  |
| occurrences causally related to treatment / all | 0 / 1  |  |  |
| deaths causally related to treatment / all      | 0 / 1  |  |  |
| Endocrine disorders                             |  |  |  |
| Adrenal insufficiency                           |  |  |  |
| subjects affected / exposed                     | 1 / 19 (5.26%)                                 |  |  |
| occurrences causally related to treatment / all | 1 / 1  |  |  |
| deaths causally related to treatment / all      | 0 / 0  |  |  |
| Infections and infestations                     |  |  |  |
| Sepsis  |  |  |  |
| subjects affected / exposed                     | 2 / 19 (10.53%)                                |  |  |
| occurrences causally related to treatment / all | 0 / 3  |  |  |
| deaths causally related to treatment / all      | 0 / 0  |  |  |
| Pneumonia                                       |  |  |  |
| subjects affected / exposed                     | 2 / 19 (10.53%)                                |  |  |
| occurrences causally related to treatment / all | 0 / 2  |  |  |
| deaths causally related to treatment / all      | 0 / 0  |  |  |
| COVID-19  |  |  |  |
| subjects affected / exposed                     | 1 / 19 (5.26%)                                 |  |  |
| occurrences causally related to treatment / all | 0 / 1  |  |  |
| deaths causally related to treatment / all      | 0 / 0  |  |  |
| Abscess bacterial                               | Additional description: abscess in gallbladder |  |  |
| subjects affected / exposed                     | 1 / 19 (5.26%)                                 |  |  |
| 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 %



| <b>Non-serious adverse events</b>   | Nivo/Ipi + SBRT and influenza vaccine  |  |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed  | 19 / 19 (100.00%)  |  |  |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 19 (5.26%)<br><br>1<br><br>1 / 19 (5.26%)<br><br>1                                 |  |  |
| Injury, poisoning and procedural complications<br>Infusion related reaction<br>subjects affected / exposed<br>occurrences (all)   | 3 / 19 (15.79%)<br><br>4   |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 2 / 19 (10.53%)<br><br>2<br><br>1 / 19 (5.26%)<br><br>1                                |  |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Fever<br>subjects affected / exposed<br>occurrences (all)<br><br>Flu like symptoms<br>subjects affected / exposed<br>occurrences (all) | 5 / 19 (26.32%)<br><br>7<br><br>1 / 19 (5.26%)<br><br>1<br><br>1 / 19 (5.26%)<br><br>1 |  |  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting  | 4 / 19 (21.05%)<br><br>6   |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry mouth</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Colitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 19 (5.26%)</p> <p>2</p> <p>2 / 19 (10.53%)</p> <p>2</p> <p>3 / 19 (15.79%)</p> <p>3</p> <p>1 / 19 (5.26%)</p> <p>1</p> |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 19 (5.26%)</p> <p>1</p>  |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash maculo-papular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>     | <p>4 / 19 (21.05%)</p> <p>5</p> <p>6 / 19 (31.58%)</p> <p>7</p> <p>3 / 19 (15.79%)</p> <p>3</p>                               |  |  |
| <p>Endocrine disorders</p> <p>Hyperthyroidism</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thyroiditis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>6 / 19 (31.58%)</p> <p>6</p> <p>1 / 19 (5.26%)</p> <p>1</p>  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>2 / 19 (10.53%)</p> <p>2</p>   |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| Myalgia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 19 (10.53%)<br>3 |  |  |
| Metabolism and nutrition disorders<br>Anorexia<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

|  |
|--|
| The study was prematurely ended as the predictive probability to meet efficacy gate (ORR 15%) was not given. |
|--|

Notes: