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
Scientific contact	Principal Investigator Inna Chen, Department of Oncology, Herlev & Gentofte Hospital, +45 38682898, inna.chen@regionh.dk

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 ≥ 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 (± 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 (± 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 (± 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 (± 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

Number of subjects in period 1	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 (± 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 (± 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 sugery og 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:

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 (± 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 (± 3 days) and once more after 6 weeks.

Primary: Objective Response Rate

End point title	Objective Response Rate[1]

End point description:

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:

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[2]			
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 occured 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 (± 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 (± 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 %

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

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

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

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: