Clinical trial results:
A Single Center, Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Gemcitabine (GEM) and Capecitabine (CAP) with or without T-ChOSTM as adjuvant therapy in patients with surgically resected pancreatic cancer

Summary

EudraCT number	2014-001163-12
Trial protocol	DK
Global end of trial date	10 July 2018

Results information

Result version number	v1 (current)
This version publication date	11 September 2020
First version publication date	11 September 2020

Trial information

Trial identification

Sponsor protocol code	GI1604

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02767752
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev University Hospital, Oncology Dept.
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Herlev University Hospital, Oncolog Dept, Herlev University Hospital, Oncology Dept., 0045 38682344, dorte.nielsen.01@regionh.dk
Scientific contact	Herlev University Hospital, Oncology Dept, Herlev University Hospital, Oncology Dept., 0045 38682344, dorte.nielsen.01@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	31 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 July 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Disease-free survival (DFS), defined as the time from the date of randomization to the date of disease recurrence determined by investigator assessment of objective radiographic disease assessments per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, or death, whichever is earlier.

Protection of trial subjects:

Patients with informed consent and fulfilling eligibility criteria were included. Continues monitoring of standard safety parameters during treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Denmark: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	5
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was opened for recruitment in December 2016 and prematurely closed for recruitment in July 2018 as modified FOLFIRINOX replaced GEM/CAP as standard of care for fit patients such as the target population for this trial. Recruitment at single site, Herlev University Hospital, Denmark

Pre-assignment

Screening details:

Eligible patients were 18 years of age or older with histologically confirmed resected ductal pancreatic adenocarcinoma with macroscopic complete resection (R0 and R1). Time from resection to treatment start <=12 weeks. Presence or history of metastatic or locally recurrent pancreatic adenocarcinoma was an exclusion criterion.

Pre-assignment period milestones

Number of subjects started	25
Intermediate milestone: Number of subjects	Screening: 25
Number of subjects completed	21

Pre-assignment subject non-completion reasons

Reason: Number of subjects	screen failure (recurrent/disseminated disease): 4

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Backbone chemotherapy (gemcitabine / capecitabine) + Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

600 mg daily for continuous oral intake until recurrence of disease

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

Dosage and administration details:

1000 mg/m² on day 1, day 8 and day 15 of every 28-days cycle (total of 6 cycles)

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

capecitabine 830 mg/m² twice daily for 21 days out of the 28 days of a treatment cycle (total of 6 cycles)

Arm title	T-ChOS

Arm description:

Backbone chemotherapy (gemcitabine/capecitabine) + T-ChOs

Arm type	Experimental
Investigational medicinal product name	T-ChOS
Investigational medicinal product code	
Other name	Benecta
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

600 mg daily for continuous oral intake until recurrence of disease

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

Dosage and administration details:

1000 mg/m² on day 1, day 8 and day 15 of every 28-days cycle (total of 6 cycles)

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

capecitabine 830 mg/m² twice daily for 21 days out of the 28 days of a treatment cycle (total of 6 cycles)

Number of subjects in period 1[1]	Placebo	T-ChOS
Started	12	9
Completed	1	9
Not completed	11	0
Unblinding at premature termination	6	-
Adverse event, non-fatal	5	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In total, 25 patients signed consent and where screened (pre-assignment period). Of those, 21 patients were eventually enrolled (treatment period) and 4 patients were screen failures (did not complete pre-assignment period)

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Backbone chemotherapy (gemcitabine / capecitabine) + Placebo	
Reporting group title	T-ChOS
Reporting group description:	
Backbone chemotherapy (gemcitabine/capecitabine) + T-ChOs	

Reporting group values	Placebo	T-ChOS	Total
Number of subjects	12	9	21
Age categorical 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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	71	68	
full range (min-max)	59 to 80	61 to 72	-
Gender categorical Units: Subjects			
Female	6	6	12
Male	6	3	9
ECOG Performance status Units: Subjects			
ECOG 0	10	6	16
ECOG 1	2	3	5
Resection status Units: Subjects			
R0	9	7	16
R1	3	2	5
Nodal status Units: Subjects			
LN+	9	8	17
LN-	3	1	4

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description:	
Backbone chemotherapy (gemcitabine / capecitabine) + Placebo	
Reporting group title	T-ChOS
Reporting group description:	
Backbone chemotherapy (gemcitabine/capecitabine) + T-ChOs	

Primary: Disease Free Survival	
End point title	Disease Free Survival
End point description:	
End point type	Primary
End point timeframe:	
measured as the time from randomization to date of local tumor recurrence, lymph node spread, distant metastases, or death from any cause.	

End point values	Placebo	T-ChOS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: months				
median (confidence interval 95%)	8.4 (0 to 21.5)	10.8 (5.9 to 15.7)		

Statistical analyses

Statistical analysis title	primary endpoint
Comparison groups	Placebo v T-ChOS
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	3.69

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

Time from randomisation to death

End point values	Placebo	T-ChOS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12[1]	9		
Units: months				
median (confidence interval 95%)	31.3 (0 to 99)	33.9 (22.3 to 45.6)		

Notes:

[1] - The CI in this group is not calculatable at time of analyse

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from signed Informed consent to 30 days after treatment stop	
Assessment type	Systematic
Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	4
Reporting groups	
Reporting group title	Placebo
Reporting group description: Backbone chemotherapy (gemcitabine / capecitabine) + Placebo	
Reporting group title	T-ChOS
Reporting group description: Backbone chemotherapy (gemcitabine/capecitabine) + T-ChOs	

Serious adverse events	Placebo	T-ChOS	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)	3 / 9 (33.33%)	
number of deaths (all causes)	6	5	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			

subjects affected / exposed	1 / 12 (8.33%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 12 (33.33%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	3 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema limbs			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	T-ChOS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	9 / 9 (100.00%)	
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 12 (66.67%)	6 / 9 (66.67%)	
occurrences (all)	9	11	

Flu-like symptoms			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
common cold			
subjects affected / exposed	0 / 12 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Fever			
subjects affected / exposed	3 / 12 (25.00%)	2 / 9 (22.22%)	
occurrences (all)	3	3	
Pain			
subjects affected / exposed	2 / 12 (16.67%)	3 / 9 (33.33%)	
occurrences (all)	4	4	
Edema limbs			
subjects affected / exposed	2 / 12 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
Injection site reaction			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Weight loss			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Investigations			
Neutropenia			
subjects affected / exposed	8 / 12 (66.67%)	7 / 9 (77.78%)	
occurrences (all)	14	26	
Thrombocytopenia			
subjects affected / exposed	2 / 12 (16.67%)	4 / 9 (44.44%)	
occurrences (all)	3	8	
Cardiac disorders			
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 12 (16.67%)	3 / 9 (33.33%)	
occurrences (all)	3	4	
Febrile neutropenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 12 (58.33%)	6 / 9 (66.67%)	
occurrences (all)	7	10	
Nausea			
subjects affected / exposed	5 / 12 (41.67%)	5 / 9 (55.56%)	
occurrences (all)	8	8	
Vomiting			
subjects affected / exposed	3 / 12 (25.00%)	2 / 9 (22.22%)	
occurrences (all)	4	3	
Anorexia			
subjects affected / exposed	7 / 12 (58.33%)	4 / 9 (44.44%)	
occurrences (all)	11	8	
Mucositis oral			
subjects affected / exposed	7 / 12 (58.33%)	5 / 9 (55.56%)	
occurrences (all)	13	9	
Hemorrhoids			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Meteorism			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	9 / 12 (75.00%)	7 / 9 (77.78%)	
occurrences (all)	22	18	
Rash			
subjects affected / exposed	4 / 12 (33.33%)	1 / 9 (11.11%)	
occurrences (all)	4	1	
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Infections and infestations			
Infections			
subjects affected / exposed	5 / 12 (41.67%)	4 / 9 (44.44%)	
occurrences (all)	8	6	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 9 (11.11%)	
occurrences (all)	1	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.

premature termination of recruitment - due to change in SOC, only 21 out of 180 planned patients included at that time

Notes: