Clinical trial results:
CONKO-006 Additive Therapie beim R1-resezierten Pankreaskarzinom mit Gemcitabin plus Sorafenib versus Gemcitabin plus Placebo über 12 Monate - eine doppelblinde, placebokontrollierte Phase IIb Studie.

A randomized double-blinded Phase IIb-Study of Additive Therapy with Gemcitabine + Sorafenib/Placebo for Patients with R1- Resection of Pancreatic cancer.

Summary

EudraCT number	2007-000718-35
Trial protocol	DE
Global end of trial date	15 July 2016

Results information

Result version number	v1 (current)
This version publication date	23 January 2022
First version publication date	23 January 2022
Summary attachment (see zip file)	Report conko 006 (Ergebnisbericht_conko-006.pdf)

Trial information

Trial identification

Sponsor protocol code	CONKO-006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Augustenburger Platz 1, Berlin, Germany, 13353
Public contact	Herr PD Dr. Helmut Oettle, Medizinische Klinik m.S. Hämatologie, Onkologie und Tumorimmunologie CVK, +49 450 553212, helmut.oettle@charite.de
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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	15 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2016
Global end of trial reached?	Yes
Global end of trial date	15 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Pancreatic cancer adjuvant therapy after R1-resectionGemcitabine plus Sorafenib vs. Gemcitabine plus Placebo is given over 12 months randomised trial, to comparate the disease free survival in both treatment groups.

Protection of trial subjects:

Secondary endpoints included overall survival (defined as the time from randomization to death from any cause), safety and treatment tolerability, and the evaluation of prognostic factors.

Background therapy:

CONKO-006 was designed as an investigator-initiated trial to improve survival in primarily resectable pancreatic cancer by the combination therapy of sorafenib +gemcitabine as compared to gemcitabine alone. Gemcitabine is the standard of care in this situation since 2007. The efficacy and safety profile of Gemcitabine is well known since its approval for advanced pancreatic cancer in the late 1990s.The combination therapy of gemcitabine + sorafenib was thought to be effective in metastatic pancreatic cancer in a phase I trial published in 2006 when the CONKO-006 trial was planned (Siu, CCR 2006). These data were not confirmed
in subsequent phase II and III trials (Cascinu, Dig Liv Dis 2014; Goncalves, Annal Oncol 2012), but the efficacy and safety profile of sorafenib+gemcitabine is therefore well known as well.

Evidence for comparator: -

Actual start date of recruitment	15 February 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	75 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 122
Worldwide total number of subjects	122
EEA total number of subjects	122

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)	98
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pancreatic cancer patients after curatively intended surgery and R1 resection

Pre-assignment

Screening details:

Main inclusion criteria
• Histological confirmed diagnosis of an adenocarcinoma of the pancreas
• Standardised surgery for tumor resection
• Result of resection: R1
For more inclusion and exclusion criteria see attachment: Ergebnisbreicht_conko-006.pdf

Period 1

Period 1 title	48 Weeks (12 cycles) treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A GemSorafenib

Arm description:

Arm A (GemSorafenib): Sorafenib 400 mg (2 tablets à 200 mg) twice daily orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28

Arm type	Experimental
Investigational medicinal product name	Sorafenib
Investigational medicinal product code	ATC Code L01XE05
Other name	Nexavar
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sorafenib 2x 200 mg twice daily orally (+ Gemcitabine 1000 mg/m² day 1, 8,15, q 29)

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Infusion

Dosage and administration details:

+ Gemcitabine 1000 mg/m² day 1, 8,15, q 28

Arm title	Arm B GemP

Arm description:

Placebo 2 tablets twice orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28;

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

Dosage and administration details:

Placebo 2x 2 tablets twice daily orally

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Infusion

Dosage and administration details:

+ Gemcitabine 1000 mg/m² day 1, 8,15, q 28

Number of subjects in period 1	Arm A GemSorafenib	Arm B GemP
Started	57	65
Completed	17	15
Not completed	40	50
premature discontinuation	40	50

Baseline characteristics

Reporting groups	
Reporting group title	Arm A GemSorafenib
Reporting group description:	
Arm A (GemSorafenib): Sorafenib 400 mg (2 tablets à 200 mg) twice daily orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28	
Reporting group title	Arm B GemP
Reporting group description:	
Placebo 2 tablets twice orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28;	

Reporting group values	Arm A GemSorafenib	Arm B GemP	Total
Number of subjects	57	65	122
Age categorical Units: Subjects			
18-85	57	65	122
Gender categorical Units: Subjects			
Female	24	27	51
Male	33	38	71
Primary tumor size Units: Subjects			
T2	2	2	4
T3	54	59	113
T4	1	4	5
Nodal status Units: Subjects			
N0	8	10	18
N+	49	55	104
Grading Units: Subjects			
G1	1	1	2
G2	32	32	64
G3	24	31	55
Unknown	0	1	1
Postoperative CA19-9			
Arm A, Median (range): 23 (1-2823); Arm B, Median (range):40 (1-11497)			
Units: Subjects			
<100	37	40	77
101-500	6	10	16
>500	5	4	9
missing	9	11	20
Karnofsky performance status			
KPS			
Units: Scale			
median	90	90	
full range (min-max)	70 to 100	60 to 100	-

End points

End points reporting groups

Reporting group title	Arm A GemSorafenib
Reporting group description:	
Arm A (GemSorafenib): Sorafenib 400 mg (2 tablets à 200 mg) twice daily orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28	
Reporting group title	Arm B GemP
Reporting group description:	
Placebo 2 tablets twice orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 28;	

Primary: recurrence-free survival (RFS)

End point title	recurrence-free survival (RFS)
End point description:	
Recurrent disease was diagnosed in 56/57 patients (98.2%) treated in GemSorafenib, and in 62/65 patients 95.3%) in GemP.	
End point type	Primary
End point timeframe:	
75 months	

End point values	Arm A GemSorafenib	Arm B GemP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	65		
Units: months				
median (full range (min-max))				
RFS	8.5 (6.6 to 10.5)	9.4 (8.3 to 10.4)		

Statistical analyses

Statistical analysis title	recurrence-free survival analysis
Comparison groups	Arm A GemSorafenib v Arm B GemP
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.73 [1]
Method	t-test, 2-sided
Confidence interval	
level	95 %
sides	1-sided

Notes:

[1] - all P-values are considered to be explorative, are two-sided and unadjusted for multiplicity, according to the trial protocol.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

75 months

Adverse event reporting additional description:

For details please find attached Report conko 006 (Table 2 (AEs maximum grade/patient), and Table 3 (SAEs)).

Assessment type	Systematic

Dictionary used

Dictionary name	CTC AE
Dictionary version	3.0

Reporting groups

Reporting group title	Gem+Sorafenib

Reporting group description: -

Reporting group title	Gem+Placebo

Reporting group description: -

Serious adverse events	Gem+Sorafenib	Gem+Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 57 (49.12%)	26 / 65 (40.00%)	
number of deaths (all causes)	3	4	
number of deaths resulting from adverse events	2	0	
Investigations			
overall	Additional description: For detailed information see Table 3 (SAEs) from the attachment Report conko 006		
subjects affected / exposed	28 / 57 (49.12%)	26 / 65 (40.00%)	
occurrences causally related to treatment / all	11 / 33	13 / 33	
deaths causally related to treatment / all	2 / 3	0 / 4	

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

Non-serious adverse events	Gem+Sorafenib	Gem+Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 57 (100.00%)	65 / 65 (100.00%)	
Investigations			
Overall	Additional description: for detailed information see table 2 attachment Report conko 006		
subjects affected / exposed	57 / 57 (100.00%)	65 / 65 (100.00%)	
occurrences (all)	855	917	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2010	Study extension

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported