Clinical trial results:
CONKO-005: Adjuvante Therapie des R0-resezierten Pankreaskarzinoms mit Gemcitabin plus Erlotinib versus Gemcitabin über 24 Wochen – eine prospektive, randomisierte, Phase III Studie

Summary

EudraCT number	2007-003813-15
Trial protocol	DE
Global end of trial date	10 July 2016

Results information

Result version number	v1 (current)
This version publication date	26 December 2021
First version publication date	26 December 2021
Summary attachment (see zip file)	Final report CONKO-005/ML20797 (Finalreport_CONKO-005_052018.pdf)

Trial information

Trial identification

Sponsor protocol code	CONKO-005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité, Campus Virchow Klinikum
Sponsor organisation address	Augustenburger Platz 1, Berlin, Germany, 13353
Public contact	Prof. Dr. med. Hanno Riess, Charité, Campus Virchow Klinikum Med. Klinik m.S. Hämat./Onkol., 030 450553013, hanno.riess@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	10 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2016
Global end of trial reached?	Yes
Global end of trial date	10 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the disease free survival (DFS) in both treatment groups and to improve survival in patients with pancreatic ductal adenocarcinoma (PDAC) and R0 resection after curatively intended surgery by the addition of the EGFR-tyrosine kinase inhibitor Erlotinib to the standard adjuvant therapy with Gemcitabine. Erlotinib had shown efficacy in metastatic pancreatic cancer patients (Moore et al. 2007) and was estimated to improve survival in primarily resectable pancreatic cancer patients as well.

Protection of trial subjects:

All data documented in the CRF that describe the population sample characteristics, efficacy and toxicity were evaluated descriptively. One prospectively defined subgroup analysis was to examine the association of EGFR-related skin rash of NCI- CTC grade ≥2 with DFS in the gemcitabine/erlotinib group. Additional subgroup analyses were planned regarding tumor size (T1/T2 vs. T3/T4), Karnofsky performance status at time of randomization (<90% vs 90–100%), CA 19-9 levels (<100 kU/l vs 101-500 kU/l vs > 500 kU/l) at study entry and start of chemotherapy (<= 6 weeks vs >6 weeks after operation).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 436
Worldwide total number of subjects	436
EEA total number of subjects	436

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)	336
From 65 to 84 years	100
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pancreatic cancer patients after curatively intended surgery and R0 resection; Further selection details for main inclusion/exclusion criteria see: Finalreport_CONKO-005.

Pre-assignment

Screening details:

436 patients were randomized by 57 study centers between April 2008 and July 2013

Period 1

Period 1 title	Treatment over 24 weeks (6 cycles) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (GemErlo)

Arm description:

Erlotinib+ Gemcitabine

Arm type	Experimental
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	n/a L01XX34
Other name	Tarceva
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Erlotinib 100 mg 1x daily orally + Gemcitabine 1000 mg/m² day 1, 8,15, q 29

Arm title	Arm B (Gem)

Arm description:

Gemcitabine

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine hydrochloride
Investigational medicinal product code	122111039
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Gemcitabine 1000 mg/m² i.v. day 1, 8, 15, q 29

Number of subjects in period 1	Arm A (GemErlo)	Arm B (Gem)
Started	219	217
Completed	145	160
Not completed	74	57
Adverse event, serious fatal	4	2
Adverse event, non-fatal	36	29
Protocol deviation	34	26

Baseline characteristics

Reporting groups	
Reporting group title	Arm A (GemErlo)
Reporting group description: Erlotinib+ Gemcitabine	
Reporting group title	Arm B (Gem)
Reporting group description: Gemcitabine	

Reporting group values	Arm A (GemErlo)	Arm B (Gem)	Total
Number of subjects	219	217	436
Age categorical Units: Subjects			
Age between 18-85	219	217	436
Age continuous Units: years			
arithmetic mean	63	65	
full range (min-max)	28 to 82	24 to 82	-
Gender categorical Units: Subjects			
Female	91	98	189
Male	128	119	247
Primary tumor size Units: Subjects			
T1/T2	27	30	57
T3/T4	192	187	379
Nodal status Units: Subjects			
N0	79	73	152
N+	140	144	284
Tumor grade Units: Subjects			
G1	8	9	17
G2	132	128	260
G3	72	74	146
Unkown	7	6	13
Time surgery to start chemotherapy			
Median (days): GemErlo 47 Gem 42			
Units: Subjects			
2-4 weeks	12	16	28
5-6 week	60	94	154
7+ weeks	139	105	244
No treatment	8	2	10
Type of surgery Units: Subjects			
Pancreatic head resection	175	180	355

Pancreatic tail resection	30	25	55
Total pancreatectomy	14	12	26
Resected in a center with Units: Subjects			
< 12 patients	115	101	216
>=12 patients	104	116	220
KPS			
Karnofsky performance status.			
Units: Scale			
median	90	90	
full range (min-max)	60 to 100	60 to 100	-
Postoperative CA 19-9			
See for more details: Online references http://www.ncbi.nlm.nih.gov/pubmed/28817370			
Units: kU/L			
median	19	18	
full range (min-max)	1 to 5816	1 to 3079	-

End points

End points reporting groups	
Reporting group title	Arm A (GemErlo)
Reporting group description: Erlotinib+ Gemcitabine	
Reporting group title	Arm B (Gem)
Reporting group description: Gemcitabine	

Primary: Disease-free survival (DFS)	
End point title	Disease-free survival (DFS)
End point description: Estimated DFS rates at 12, 24, and 60 months were 48%, 25%, and 12% (47%, 26%, and 13% in the GemErlo arm; 48%, 25%, and 11% in the Gem arm).	
End point type	Primary
End point timeframe: From baseline to month 60	

End point values	Arm A (GemErlo)	Arm B (Gem)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	217		
Units: Months				
median (full range (min-max))				
95% confidence interval	11.4 (9.6 to 13.2)	11.4 (9.2 to 13.6)		

Attachments (see zip file)	DFS and OSP/10.1200-JCO.2017.72.6463Figure2.pdf

Statistical analyses

Statistical analysis title	Calculation of the sample size (exponential model)
Statistical analysis description: The primary endpoint disease-free survival was defined as time from randomization to first recurrence of disease or death from any cause. The test for significance was based on the log-rank test, for a one-sided significance level of 5% with a power of 80%.	
Comparison groups	Arm A (GemErlo) v Arm B (Gem)

Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.26 [2]
Method	t-test, 2-sided
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - the analysis of the primary end point was tested one sided

[2] - All P values were two-sided and unadjusted, according to the trial protocol.

Secondary: DFS and OS for Different CA 19-9 Levels After Surgery

End point title	DFS and OS for Different CA 19-9 Levels After Surgery

End point description:

Disease-Free Survival (DFS); Overall Survival (OS);
For 336 patients with cancer antigen 19-9 (CA 19-9) levels <=100 kU/L (167 patients in the GemErlo arm and 169 in the Gem arm), median DFS was 12.2 months in the GemErlo arm versus 13.1 months in the Gem arm (P = .626); median OS was 27.6 versus 30.1 months (P = .849). Fifty-four patients with postoperatively increased CA 19-9 had a significantly reduced median DFS and OS (P , .001); this effect was comparable in both arms. (Table 3. Diseaseas-Free Survival and Overall Survial for Different CA 19-9 Levels After Surgery; Fig 3. (A) Disease-free survival and (B) overall survival for different CA 19-9 levels after surgery.

End point type	Secondary

End point timeframe:

from baseline to month 60

End point values	Arm A (GemErlo)	Arm B (Gem)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	217		
Units: Months				
median (full range (min-max))				
Median DFS <= 100	12.2 (9.8 to 14.5)	13.1 (10.6 to 15.6)		
Median DFS 101 to 500	6.0 (4.2 to 7.8)	9.0 (6.3 to 11.7)		
Median DFS >500	5.5 (0.5 to 10.45)	3.2 (0 to 7.4)		
Median OS <= 100	27.6 (22.7 to 32.5)	30.1 (26.3 to 33.8)		
Median OS 101 to 500	15.6 (10 to 21.2)	16.4 (15.2 to 17.7)		
Median OS >500	9.3 (9.2 to 9.5)	11.9 (0 to 27.3)		

Attachments (see zip file)	(A) Disease-free survival and (B) overall survival/10.1200-JCO. Disease-Free Survival and Overall Survival for Dif/table3.jpeg

Statistical analyses

Statistical analysis title	Survival probability estimated with the Kaplan-Mei

Statistical analysis description:

The test for significance was based on the log-rank test, for a one-sided significance level of 5% with a power of 80%.

Comparison groups	Arm A (GemErlo) v Arm B (Gem)
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	equivalence[3]
P-value	= 0.26
Method	Logrank
Confidence interval	
level	95 %
sides	1-sided

Notes:

[3] - A sample size of 436 patients was
required to detect an improvement in median DFS of 4 months with
GemErlo, with a statistical power of 80% and one-sided 5% type I error,
and assuming a 10% dropout rate, a 4-year recruitment period, and
a follow-up of at least 3 years.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline to 60 months	
Adverse event reporting additional description:	
For detailed AE and SAE see attachment "Final report CONKO-005/ML20797"(Table 2 AE and Table 3 SAE).	
Assessment type	Systematic

Dictionary used	
Dictionary name	own
Dictionary version	1

Reporting groups	
Reporting group title	Arm A GemErlo
Reporting group description: -	
Reporting group title	Arm B Gem
Reporting group description: -	

Serious adverse events	Arm A GemErlo	Arm B Gem	
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 219 (31.05%)	56 / 217 (25.81%)	
number of deaths (all causes)	4	3	
number of deaths resulting from adverse events	1	0	
Investigations			
Overall	Additional description: All serious adverse events were merged.		
alternative assessment type: Non-systematic			
subjects affected / exposed	68 / 219 (31.05%)	56 / 217 (25.81%)	
occurrences causally related to treatment / all	8 / 83	17 / 76	
deaths causally related to treatment / all	1 / 4	0 / 3	

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

Non-serious adverse events	Arm A GemErlo	Arm B Gem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	208 / 219 (94.98%)	211 / 217 (97.24%)	
Investigations			
Overall	Additional description: All none-serious advers events were merged.		
alternative assessment type: Non-systematic			

subjects affected / exposed occurrences (all)	208 / 219 (94.98%) 6444	211 / 217 (97.24%) 6772	

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28817370