Clinical trial results:
Prospective multicenter phase III clinical trial using cytoreductive surgery with hyperthermic intraoperative chemotherapy (HIPEC) after preoperative chemotherapy in patients with peritoneal carcinomatosis of gastric cancer incl. adenocarcinoma of the esophagogastreal junction

Summary

EudraCT number	2006-006088-22
Trial protocol	DE
Global end of trial date	09 June 2020

Results information

Result version number	v1 (current)
This version publication date	29 June 2022
First version publication date	29 June 2022
Summary attachment (see zip file)	Report (Gastripec_Ergebnisbericht_final1.0_2021-12-03_unterschrieben.pdf)

Trial information

Trial identification

Sponsor protocol code	Gastripec-I

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02158988
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité Berlin
Sponsor organisation address	Universitätsmedizin Berlin, Berlin, Germany,
Public contact	Beate Rau, Chirurgie, Charité Campus Virchow-Klinikum, 0049 (0)30450 622 214, beate.rau@charite.de
Scientific contact	Beate Rau, Chirurgie, Charité Campus Virchow-Klinikum, 0049 (0)30450 622 214, beate.rau@charite.de

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	03 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 June 2020
Global end of trial reached?	Yes
Global end of trial date	09 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy of hyperthermic intraoperative chemotherapy (HIPEC) (extension of survival starting at randomisation) by combination of pre-and postoperative chemotherapy + cytoreductive surgery and HIPEC compared to pre-and postoperative chemotherapy + cytoreductive surgery without HIPEC

Protection of trial subjects:

Patient safety is ensured on the one hand by the collection of the secondary endpoint "30-day complication rate after cytoductive surgery with or without HIPEC" and on the other hand by regular examinations during study therapy and at a maximum interval of 3 months in follow-up.
The study therapy is continued for the individual patient in a dose-limited manner or, if necessary, discontinued if there is serious dose-limiting toxicity or remittent severe adverse events that can be attributed to the study treatment.

Background therapy: -

Evidence for comparator:

Treatment with cytoreductive surgery (ZRC) and hyperthermic intraperitoneal chemotherapy (HIPEC) expects a significant increase in survival time. The decision to use cytoductive surgery is based on the idea of maximum tumor load reduction, which brings with it an improved response to intraperitoneal chemotherapy as well as the reduced likelihood of passage disorder due to intra-abdominal tumor progression. In order to create the best possible conditions for this, all patients are chemotheraped preoperatively before the main procedure.

Actual start date of recruitment	04 March 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research, Safety
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 105
Worldwide total number of subjects	105
EEA total number of subjects	105

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)	78
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with gastric cancer incl. adenocarcinoma of the esophagogastreal junction and peritoneal carcinomatosis without any distant metastases with exception of Krukenberg tumors were recruited from March 2014 to June 2018

Pre-assignment

Screening details:

282 patients were screened
Peritoneal staging and the possibility of reduction (80% of the tumour) in line with zytoreductive surgery was evaluated at screening.

Period 1

Period 1 title	overall trial (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

Arm description:

No HIPEC

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

Dosage and administration details:

Patients with negative or unknown HER-2 status received
50 mg/m2 i.v. (max. 100 mg), Day 1
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients with negative or unknown HER-2 status received
130 mg/m2 i.v. (max. 260 mg), Day 1
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

Investigational medicinal product name	Capecitabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients with negative or unknown HER-2 status received
625 mg/m2 p.o. (2x daily., max. 2500 mg total), Day 1-21
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

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

Dosage and administration details:

Patients with POSITVE HER-2 status received
80 mg/m² i.v. Day 1 (max. 160 mg)
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

Investigational medicinal product name	Capecitabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients with POSISIVE HER-2 status received
1000 mg/m2 p.o. (2x daily, max. 4000 mg total), Day 1-14
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients with POSITIVE HER-2 status received
8 mg/kg i.v. Day 1 (first cycle, from second cycle 6 mg/kg)
In 3 cycles of chemotherapy (2-3 weeks after the end of the last cycle) before cytotorductive surgery and 3 cycles of postoperative systemic chemotherapy (2-3 weeks after the end of the last cycle) 4-12 weeks after surgery

Arm title	Arm B

Arm description:

HIPEC

Arm type	Experimental
Investigational medicinal product name	Mitomycin C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intraperitoneal use

Dosage and administration details:

15 mg/m2 (max. 30 mg, max. 5 L Perfusat) intraoperative

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for infusion
Routes of administration	Intraperitoneal use

Dosage and administration details:

75 mg/m2 (max. 150 mg, max. 5 L Perfusat) intraoperative

Number of subjects in period 1	Arm A	Arm B
Started	53	52
Completed	53	52

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
No HIPEC	

Reporting group title	Arm B
Reporting group description:	
HIPEC	

Reporting group values	Arm A	Arm B	Total
Number of subjects	53	52	105
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	40	38	78
From 65-84 years	13	14	27
85 years and over	0	0	0
Gender categorical Units: Subjects			
female	24	23	47
male	29	29	58

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
No HIPEC	

Reporting group title	Arm B
Reporting group description:	
HIPEC	

Primary: Primary end point

End point title	Primary end point[1]
End point description:	

End point type	Primary
End point timeframe:	
Randomisation until last patient out	

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: For a full description of the trial analyses, please see trial synopsis, uploaded together with the posting of this results report.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	22	27		

Statistical analyses

No statistical analyses for this end point

Secondary: 30-days complication rate

End point title	30-days complication rate
End point description:	
30-days complication rate after cytoreductive surgery with or withour HIPEC	

End point type	Secondary
End point timeframe:	
30 days after cytoreductive surgery	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	53	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progress

End point title	Time to progress

End point description:

Time to verifiable progress of tumor

End point type	Secondary

End point timeframe:

From randomisation to last patient out

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	35	36		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to metastases

End point title	Time to metastases

End point description:

Time of appearance of elsewhere localised metastases

End point type	Secondary

End point timeframe:

From randomisation to last patient out

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	49		
Units: whole	34	31		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life

End point description:

Quality of life

End point type	Secondary

End point timeframe:

Before surgery, begin of 4th chemotherapy cycle, begin of 6th cheomtherapy cycle, Follow-up 3 months after end of therapy, Follow-up 6 months after end of therapy

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	53	52		

Statistical analyses

No statistical analyses for this end point

Secondary: toxicity and adverse events

End point title	toxicity and adverse events

End point description:

Frequency of toxicity and adverse events

End point type	Secondary

End point timeframe:

From begin of treatment to last patient out

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	38	42		

Statistical analyses

No statistical analyses for this end point

Secondary: surgical and therapeutic intervention

End point title	surgical and therapeutic intervention

End point description:

Frequency of required surgical and therapeutic intervention

End point type	Secondary

End point timeframe:

After cytoreductive surgery upto 2.5 years

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[2]	28[3]		
Units: whole	4	5		

Notes:

[2] - Numbers given exclusively for patients with complete cyto reduction

[3] - Numbers given exclusively for patients with complete cyto reduction

Statistical analyses

No statistical analyses for this end point

Secondary: hospitalization

End point title	hospitalization

End point description:

Duration of total hospitalization

End point type	Secondary

End point timeframe:

During 2.5 years after randomisation

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	52		
Units: whole	53	51		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Start of treatment until last performed follow-Up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Please see the list of AEs related and not related to the IMP in the trial synopsis, uploaded together with the posting of this results report.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2013	Change of coordinating investigator biobanking added Change in the composition of the DMC Change in selection criteria Change in tehrapy for HER-2 positive patients Some changes in definitions

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported