Clinical trial results:
INTRAPERITONEAL AEROSOLISATION OF ALBUMIN-STABILIZED PACLITAXEL NANOPARTICLES FOR PERITONEAL CARCINOMATOSIS – PHASE I/II STUDY PROTOCOL

Summary

EudraCT number	2017-001688-20
Trial protocol	BE DK
Global end of trial date	29 November 2020

Results information

Result version number	v1 (current)
This version publication date	11 March 2022
First version publication date	11 March 2022

Trial information

Trial identification

Sponsor protocol code	AGO/2017/003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03304210
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Ghent
Sponsor organisation address	Corneel Heymanslaan 10, Ghent, Belgium, 9000
Public contact	HIRUZ, Ghent University Hospital, +32 93320500, karen.demeuleneir@uzgent.be
Scientific contact	HIRUZ, Ghent University Hospital, 093325524 93320500, karen.demeuleneir@uzgent.be

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	06 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 May 2020
Global end of trial reached?	Yes
Global end of trial date	29 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the safety and efficacy of IV Taxol combined with repeated pressurized intraperitoneal aerosol therapy (PIPAC) using albumin bound nanoparticle paclitaxel (nab-pac, Abraxane) in a multicentre, multinational phase I/II trial.

Protection of trial subjects:

Ethics review and approval, informed consent. The study followed a time-to-event continual reassessment model (TITE-CRM)
The DMC (Data Safety Monitoring Committee) will, based on independent assessment of trial data as they become available, safeguard patient safety and trial integrity. The DMC will take decisions on trial continuation, protocol adaptation, or discontinuation based on efficacy or futility.
Adverse events will be reported between the first PIPAC and 30 after the last PIPAC procedure. All AEs and SAE's will be recorded in the patient's file and in the CRF. All SAE's will be reported as described below.
Medical events that occur between signing of the Informed Consent and the first intake of trial medication will be documented on the medical and surgical history section and concomitant diseases page of the CRF.
SAE's occurring within a period of 30 days following the last intake of trial medication will also be handled as such if spontaneously reported to the investigator.
All serious adverse events (SAE) and pregnancies occurring during clinical trials must be reported by the local Principal Investigator and local Ethical Committee within 2 working days after becoming aware of the SAE. This reporting is done by using the appropriate SAE form. It is the responsibility of the local Principal Investigator to report the local SAE's to the local EC.
In case the investigator decides the SAE is a SUSAR (Suspected Unexpected Serious Adverse Reaction), Bimetra Clinics will report the SUSAR to the Central EC and the CA within the timelines as defined in national legislation. The National Coordinating Investigator reports the SUSAR to all National Coordinating Investigators.
In case of a life-threatening SUSAR the entire reporting process must be completed within 7 calendar days. In case of a non-life-threatening SUSAR the reporting process must completed within 15 calendar days.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Belgium: 19
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	15
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Thirty-one patients were assessed for eligibility and signed the informed consent form. Between September 2017 and March 2020, treatment was initiated in 23 eligible patients at Ghent University Hospital (n=22) and at Odense University Hospital (n=1). Twenty of them underwent at least two consecutive PIPAC treatments

Pre-assignment

Screening details:

Inclusion criteria and exclusion criteria

Pre-assignment period milestones

Number of subjects started	20
Number of subjects completed	20

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Abraxane 35 mg/m²

Arm description:

PIPAC with Abraxane (35 mg/m²) will be administered every 4 weeks for 3 cycles.
PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.

Arm type	Experimental
Investigational medicinal product name	abraxane
Investigational medicinal product code	PR1
Other name	Albumin bound nanoparticle paclitaxel
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Abraxane 35 mg/m²
Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique.

Arm title	Abraxane 70 mg/m²

Arm description:

PIPAC with Abraxane (70 mg/m²) will be administered every 4 weeks for 3 cycles.
PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.

Arm type	Experimental
Investigational medicinal product name	abraxane
Investigational medicinal product code	PR1
Other name	Albumin bound nanoparticle paclitaxel
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Abraxane 70 mg/m²
Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique.

Arm title	Abraxane 90 mg/m²

Arm description:

PIPAC with Abraxane (90 mg/m²) will be administered every 4 weeks for 3 cycles.
PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.

Arm type	Experimental
Investigational medicinal product name	abraxane
Investigational medicinal product code	PR1
Other name	Albumin bound nanoparticle paclitaxel
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Abraxane 90 mg/m²
Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique.

Arm title	Abraxane 112.5 mg/m²

Arm description:

PIPAC with Abraxane (112.5 mg/m²) will be administered every 4 weeks for 3 cycles.
PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.

Arm type	Experimental
Investigational medicinal product name	abraxane
Investigational medicinal product code	PR1
Other name	Albumin bound nanoparticle paclitaxel
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Abraxane 112.5 mg/m²
Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique.

Arm title	Abraxane 140 mg/m²

Arm description:

PIPAC with Abraxane (140 mg/m²) will be administered every 4 weeks for 3 cycles.
PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.

Arm type	Experimental
Investigational medicinal product name	abraxane
Investigational medicinal product code	PR1
Other name	Albumin bound nanoparticle paclitaxel
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Abraxane 140 mg/m²
Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique.

Number of subjects in period 1	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²
Started	2	2	3
Completed	2	2	3

Number of subjects in period 1	Abraxane 112.5 mg/m²	Abraxane 140 mg/m²
Started	3	10
Completed	3	10

Baseline characteristics

Reporting groups	
Reporting group title	Abraxane 35 mg/m²
Reporting group description:	
PIPAC with Abraxane (35 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	
Reporting group title	Abraxane 70 mg/m²
Reporting group description:	
PIPAC with Abraxane (70 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	
Reporting group title	Abraxane 90 mg/m²
Reporting group description:	
PIPAC with Abraxane (90 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	
Reporting group title	Abraxane 112.5 mg/m²
Reporting group description:	
PIPAC with Abraxane (112.5 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	
Reporting group title	Abraxane 140 mg/m²
Reporting group description:	
PIPAC with Abraxane (140 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Reporting group values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²
Number of subjects	2	2	3
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)	1	0	3
From 65-84 years	1	2	0
85 years and over	0	0	0
Age continuous Units: years			
median	64	68	52
full range (min-max)	62 to 65	67 to 68	49 to 58

Gender categorical Units: Subjects			
Female	1	2	0
Male	1	0	3

Reporting group values	Abraxane 112.5 mg/m²	Abraxane 140 mg/m²	Total
Number of subjects	3	10	20
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)	2	9	15
From 65-84 years	1	1	5
85 years and over	0	0	0
Age continuous Units: years			
median	59	51	
full range (min-max)	47 to 70	28 to 66	-
Gender categorical Units: Subjects			
Female	2	7	12
Male	1	3	8

End points

End points reporting groups

Reporting group title	Abraxane 35 mg/m²
Reporting group description:	
PIPAC with Abraxane (35 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Reporting group title	Abraxane 70 mg/m²
Reporting group description:	
PIPAC with Abraxane (70 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Reporting group title	Abraxane 90 mg/m²
Reporting group description:	
PIPAC with Abraxane (90 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Reporting group title	Abraxane 112.5 mg/m²
Reporting group description:	
PIPAC with Abraxane (112.5 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Reporting group title	Abraxane 140 mg/m²
Reporting group description:	
PIPAC with Abraxane (140 mg/m²) will be administered every 4 weeks for 3 cycles. PIPAC with Abraxane: Albumin bound nanoparticle paclitaxel (Abraxane) will be administered intraperitoneally using the PIPAC technique. The administered dose will escalate ranging from 35 to 140 mg/m². PIPAC will be performed every 4 weeks for 3 cycles.	

Primary: Maximally Tolerated Dose (MTD) of Abraxane

End point title	Maximally Tolerated Dose (MTD) of Abraxane[1]
End point description:	
Dose limiting toxicities will be monitored.	

End point type	Primary
End point timeframe:	
Within 14 weeks of the start of the treatment	

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: NA

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: toxicities				
Abraxane 35 mg/m²	2	0	0	0
Abraxane 70 mg/m²	0	2	0	0

Abraxane 90 mg/m²	0	0	3	0
Abraxane 112.5 mg/m²	0	0	0	3
Abraxane 140 mg/m²	0	0	0	0

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: toxicities				
Abraxane 35 mg/m²	0			
Abraxane 70 mg/m²	0			
Abraxane 90 mg/m²	0			
Abraxane 112.5 mg/m²	0			
Abraxane 140 mg/m²	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Surgical Morbidity Will be Measured

End point title	Surgical Morbidity Will be Measured
End point description:	
This will be estimated with the Dindo-Clavien classification	
End point type	Secondary
End point timeframe:	
6 months after third PIPAC	

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: morbidity	2	2	3	3

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: morbidity	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration of Abraxane

End point title	Maximum Plasma Concentration of Abraxane

End point description:

Abraxane will be measured in plasma, using UPLC-MS/MS.

End point type	Secondary

End point timeframe:

T = 0 minutes, T = 15 minutes, T = 30 minutes, T = 60 minutes, T = 1.5 hour, T = 2 hours, T = 4 hours, T = 8 hours, T = 12 hours, T = 24 hours

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: ng/mL*h				
median (standard deviation)	58 (± 15)	138 (± 42)	101 (± 13)	157 (± 49)

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ng/mL*h				
median (standard deviation)	184 (± 68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Curve (AUC) of Abraxane

End point title	Area Under The Curve (AUC) of Abraxane

End point description:

Abraxane will be measured in plasma, using LC-MS/MS.

End point type	Secondary

End point timeframe:

T = 0 minutes, T = 15 minutes, T = 30 minutes, T = 60 minutes, T = 1.5 hour, T = 2 hours, T = 4 hours, T = 8 hours, T = 12 hours, T = 24 hours

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: ng/mL*h				
median (standard deviation)	585 (± 93)	962 (± 237)	813 (± 99)	1658 (± 465)

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ng/mL*h				
median (standard deviation)	2002 (± 569)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics (PD) of Abraxane Will be Analysed Using Biomarkers

End point title	Pharmacodynamics (PD) of Abraxane Will be Analysed Using Biomarkers

End point description:

Tumour markers will be analysed - CA15.3 in case of breast cancer, CEA in case of stomach cancer, CA19.9 in case of pancreatic cancer, CA125 in case of ovarian cancer.

End point type	Secondary

End point timeframe:

T = 0 weeks, T = 1 week for every PIPAC

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: regression based on tumor marker				
number (not applicable)	0	0	1	1

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: regression based on tumor marker				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics (PD) of Abraxane Will be Analyzed by Tumour Biopsies

End point title	Pharmacodynamics (PD) of Abraxane Will be Analyzed by Tumour Biopsies

End point description:

Tumour samples will be collected (5x5x5 mm³) at the end of the aerosol delivery after each PIPAC procedure.

End point type	Secondary

End point timeframe:

T = 30 minutes

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: regression based on PRGS				
number (not applicable)	1	1	1	1

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: regression based on PRGS				
number (not applicable)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life (The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC QLQ-C30)

End point title	Quality of Life (The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC QLQ-C30)

End point description:

This will be investigated using the EORTC QLQ-C30 questionnaire. As to question 1 to 28: the scale varies from 1 (not at all) to 4 (very much). A higher value indicates a lower quality of life. The total score will be between 28 and 112.
The scale of question 29 and 30 varies from 1 (very poor) to 7 (excellent). The higher the value, the better the quality of life. The total score will be between 2 and 14.
If reporting a score on a scale, please include the unabbreviated scale title, the minimum and maximum values, and whether higher scores mean a better or worse outcome.

End point type	Secondary

End point timeframe:

Pre-operatively (every PIPAC), week 2 (every PIPAC) and, month 2 and month 6 (after the third PIPAC)

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: improved global health status after 6m				
number (not applicable)	2	0	3	3

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: improved global health status after 6m				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life (Functional Assessment of Cancer Therapy, FACT-G Questionnaire)

End point title	Quality of Life (Functional Assessment of Cancer Therapy, FACT-G Questionnaire)

End point description:

This will be investigated using the FACT-G questionnaire. The scale of all questions varies from 0 (not at all) to 4 (very much). The total score will be between 0 and 108. The lower the total score, the better the quality of life.
If reporting a score on a scale, please include the unabbreviated scale title, the minimum and maximum values, and whether higher scores mean a better or worse outcome.

End point type	Secondary

End point timeframe:

Pre-operatively (every PIPAC), week 2 (every PIPAC) and, month 2 and month 6 (after the third PIPAC)

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: improved global health status after 6m				
number (not applicable)	2	0	3	3

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: improved global health status after 6m				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Neutropenia - Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE v4.0

End point title	Neutropenia - Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE v4.0

End point description:

Blood samples will be collected to analyse the absolute neutrophil count

End point type	Secondary

End point timeframe:

Pre-operatively, and 12 hours, 24 hours and 1 week after each PIPAC

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: participants				
CTCAE grade <=2	0	0	1	1
CTCAE grade >2	0	0	0	0
no neutropenia	2	2	2	2

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: participants				
CTCAE grade <=2	4			
CTCAE grade >2	1			
no neutropenia	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Decreased Platelets - Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE v4.0

End point title	Decreased Platelets - Number of Participants With Treatment-related Adverse Events as Assessed by CTCAE v4.0

End point description:

Blood samples will be collected to analyse the amount of platelets.

End point type	Secondary

End point timeframe:

Pre-operatively, and 12 hours, 24 hours and 1 week after each PIPAC

End point values	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²	Abraxane 112.5 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	3	3
Units: Count of Participants				
CTCAE grade <=2	0	1	1	2
CTCAE grade >2	0	0	1	0
no thrombopenia	2	1	1	1

End point values	Abraxane 140 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Count of Participants				
CTCAE grade <=2	3			
CTCAE grade >2	0			
no thrombopenia	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 months	
Adverse event reporting additional description:	
NA	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	NA
Dictionary version	NA

Reporting groups	
Reporting group title	Abraxane 35 mg/m²
Reporting group description: -	
Reporting group title	Abraxane 70 mg/m²
Reporting group description: -	
Reporting group title	Abraxane 90 mg/m²
Reporting group description: -	
Reporting group title	Abraxane 112.5 mg/m²
Reporting group description: -	
Reporting group title	Abraxane 140 mg/m²
Reporting group description: -	

Serious adverse events	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	2 / 3 (66.67%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
anaphylactic shock during surgery			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
surgical wound infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
thrombocytopenia grade 3 (CTCAE)			

subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
anorexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
progression peritoneal disease leading to death			
subjects affected / exposed	1 / 2 (50.00%)	2 / 2 (100.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
intestine obstruction			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Redness			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
infection peritoneum			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Abraxane 112.5 mg/m²	Abraxane 140 mg/m²	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	6 / 10 (60.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			

anaphylactic shock during surgery			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
surgical wound infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
thrombocytopenia grade 3 (CTCAE)			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
anorexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
progression peritoneal disease leading to death			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
intestine obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Redness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
infection peritoneum			

subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Abraxane 35 mg/m²	Abraxane 70 mg/m²	Abraxane 90 mg/m²
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
hypertension			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
electrocardiogram T wave abnormal			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
bleeding at incision			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
surgical wound infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Nervous system disorders			
peripheral sensory neuropathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
thrombopenia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
white blood cell decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
edema lower limbs			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
allergic reaction to anesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
adhesions			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
diarrhea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
paralytic ileus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
vomiting			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
bacterial pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
alopecia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
hyperhidrosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
skin infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
peritoneal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
elevated ALP			
subjects affected / exposed	0 / 2 (0.00%)	2 / 2 (100.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
elevated ALT			
subjects affected / exposed	1 / 2 (50.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)
occurrences (all)	1	2	3
elevated AST			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)
occurrences (all)	2	2	3
elevated GGT			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
elevated bilirubin			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
hyperglycemia			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
hyperkalemia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 2 (100.00%)	2 / 3 (66.67%)
occurrences (all)	0	2	2
hypernatremia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
hypokalemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Abraxane 112.5 mg/m²	Abraxane 140 mg/m²	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	10 / 10 (100.00%)	
Vascular disorders			
hypertension			
subjects affected / exposed	1 / 3 (33.33%)	7 / 10 (70.00%)	
occurrences (all)	1	7	
Cardiac disorders			
electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
bleeding at incision			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
surgical wound infection			
subjects affected / exposed	1 / 3 (33.33%)	4 / 10 (40.00%)	
occurrences (all)	1	4	
Nervous system disorders			
peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	2 / 3 (66.67%)	9 / 10 (90.00%)	
occurrences (all)	2	9	
neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	5 / 10 (50.00%)	
occurrences (all)	1	5	
thrombopenia			

subjects affected / exposed	2 / 3 (66.67%)	3 / 10 (30.00%)	
occurrences (all)	2	3	
white blood cell decreased			
subjects affected / exposed	2 / 3 (66.67%)	3 / 10 (30.00%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
edema lower limbs			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Immune system disorders			
allergic reaction to anesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	3	
adhesions			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
diarrhea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
nausea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
paralytic ileus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
bacterial pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders			
alopecia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
skin infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Infections and infestations			
peritoneal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
elevated ALP			
subjects affected / exposed	2 / 3 (66.67%)	4 / 10 (40.00%)	
occurrences (all)	2	4	
elevated ALT			
subjects affected / exposed	2 / 3 (66.67%)	4 / 10 (40.00%)	
occurrences (all)	2	4	
elevated AST			
subjects affected / exposed	2 / 3 (66.67%)	6 / 10 (60.00%)	
occurrences (all)	2	6	
elevated GGT			
subjects affected / exposed	2 / 3 (66.67%)	7 / 10 (70.00%)	
occurrences (all)	2	7	
elevated bilirubin			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
hyperglycemia			
subjects affected / exposed	1 / 3 (33.33%)	8 / 10 (80.00%)	
occurrences (all)	1	8	
hyperkalemia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 10 (30.00%)	
occurrences (all)	1	3	
hypernatremia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
hypokalemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2018	- The number of patients that will be included in University Hospital Ghent during phase I will be increased to (maximum) 20. Inclusion in the other participating centers (outside Belgium) is difficult, in contrast to the inclusion in University Hospital Ghent. Therefore, a maximum of approximately 20 patients will be included in University Hospital Ghent instead of the first 7 patients foreseen. The exact number will depend on eventual inclusion by the other participating centers. – Patients with breast cancer and upper GI cancer were added to the inclusion criteria. Literature demonstrates effectiveness of systemic administration of Abraxane in these types of tumors. – Patients for whom alternative systemic treatments are still an option were also added to the inclusion criteria. Offering our study only to patients without alternative systemic options (so-called end-of-treatment patients) will make inclusion enormously difficult, as this group of patients will then be in a virtually palliative setting, which means that they have insufficient life expectancy and are also physically too weak to undergo general anesthesia in combination with intraperitoneal administration to undergo. Parallel administration of chemotherapy containing a taxane (paclitaxel or docetaxel) is an exclusion criterion. – Consequently, we also like to change the title to: "Intraperitoneale aerosolvorming van albumine-gestabiliseerde paclitaxel nanopartikels (Abraxane®) voor de behandeling van buikvlieskanker: een fase I/II klinische studie" in Dutch and "Intraperitoneal aerosolisation of albumin-stabilized paclitaxel nanoparticles for peritoneal carcinomatosis – phase I/II study protocol" in English. – In addition, we would like to collect additional plasma samples from patients during phase I, in function of systemic toxicity assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported