Clinical trial results:
Treatment of peritoneal carcinomatosis with Pressurized IntraPeritoneal Aerosol Chemotherapy

- PIPAC-2 trial -

Summary

EudraCT number	2016-003394-18
Trial protocol	DK
Global end of trial date	20 January 2022
Results information	
Result version number	v1 (current)
This version publication date	17 May 2023
First version publication date	17 May 2023

Trial information

Trial identification	
Sponsor protocol code	PIPAC2trial
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03287375
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J.B. Winsloews Vej 4, Odense, Denmark, 5000
Public contact	Surgical Department A, Odense University Hospital, 45 65411857, ouh.ode.a.pipac@rsyd.dk
Scientific contact	Surgical Department A, Odense University Hospital, 45 65411857, ouh.ode.a.pipac@rsyd.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	16 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2022
Global end of trial reached?	Yes
Global end of trial date	20 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify if PIPAC (Pressurized IntraPeritoneal Aerosol Chemotherapy) can induce major/complete response (PRGS 1+2), based on repeated peritoneal biopsies, within a series of three PIPAC procedures.

Protection of trial subjects:

Conducted in accordance with Helsinki Declaration. Approved by the IRB. Monitored by the Good Clinical Practice Unit at Odense University Hospital

Background therapy:

Not relevant

Evidence for comparator:

Not relevant

Actual start date of recruitment	01 September 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: 110
Worldwide total number of subjects	110
EEA total number of subjects	110

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)	60
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruited based on decisions at the dedicated multidisciplinary team conference

Pre-assignment

Screening details:

The study planned to include 137 patients, but ended up with 143 patients. 33 of these were included in an ePIPAC amendment approved by the Ethical Committee (publications attached), and therefore the total number of patients in thie results database is 110.
Of these 110, 62 completed all 3 PIPACs and were thus amenable for primary endpoint eval.

Period 1

Period 1 title	Study period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Investigational

Arm description:

Patients receiving PIPAC

Arm type	Experimental
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intraabdominal use

Dosage and administration details:

92 mg/m2 in 150 ml dextrose

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intraabdominal use

Dosage and administration details:

7.5 mg/m2 in 150 ml saline

Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intraabdominal use

Dosage and administration details:

1.5 mg/m2 in 50 ml saline

Number of subjects in period 1	Investigational
Started	110
Completed	62
Not completed	48
Adverse event, serious fatal	4
Physician decision	44

Baseline characteristics

Reporting groups

Reporting group title	Study period

Reporting group description: -

Reporting group values	Study period	Total	
Number of subjects	110	110	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	60	60	
From 65-84 years	50	50	
85 years and over	0	0	
Age continuous Units: years			
median	63		
full range (min-max)	34 to 80	-	
Gender categorical Units: Subjects			
Female	66	66	
Male	44	44	

End points

End points reporting groups

Reporting group title	Investigational
Reporting group description:	
Patients receiving PIPAC	

Primary: No. patients with histological regression (PRGS 1-2)

End point title	No. patients with histological regression (PRGS 1-2)[1]
End point description:	
End point type	Primary
End point timeframe:	
After 3 PIPACs	

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: This is merely decriptive data including a ratio, no advanced statistics were applied. Please consult the published article for more details.

End point values	Investigational			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: no. patients	110			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first intervention to 30 days after the last PIPAC	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	Intervention arm
Reporting group description: Per procedure (n=336)	

Serious adverse events	Intervention arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 110 (3.64%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	1		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Cancer with a high tumour mutational burden	Additional description: Progressive disease		
subjects affected / exposed	3 / 110 (2.73%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		

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

Non-serious adverse events	Intervention arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 110 (17.27%)		
Gastrointestinal disorders			

Pain assessment	Additional description: Grade 3 or higher		
subjects affected / exposed	8 / 110 (7.27%)		
occurrences (all)	8		
Constipation	Additional description: Grade 3 or higher		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences (all)	2		
Ileus	Additional description: Grade 3 or higher		
subjects affected / exposed	6 / 110 (5.45%)		
occurrences (all)	6		
Nausea	Additional description: Grade 3 or higher		
subjects affected / exposed	3 / 110 (2.73%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2018	Application of one minute of electrostatic precipitation (ePIPAC) in 33 patients. This amendment was approved by the ethics committee, and did not alter the IMPs.

Notes:

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.

The publications are divided in the PIPAC-OPC2 study (n=110) (PMID: 36602663) and the amendment of ePIPAC with one minute of electrostatic precipitation (n=33) (PMID: 31493986)

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36602663

http://www.ncbi.nlm.nih.gov/pubmed/31493986