



**Clinical trial results:**

**A pilot trial of PEGPH20 (pegylated hyaluronidase) in combination with avelumab (anti-PD-L1 MSB0010718C) in chemotherapy resistant pancreatic cancer**

**Summary**

EudraCT number	2016-004603-31
Trial protocol	ES
Global end of trial date	25 January 2019

**Results information**

Result version number	v1 (current)
This version publication date	31 January 2020
First version publication date	31 January 2020

**Trial information**

**Trial identification**

Sponsor protocol code	PH1603
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03481920
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	PH Research
Sponsor organisation address	General Díaz Porlier 61, 4-3, Madrid, Spain, 28006
Public contact	Clinical Trial Coordinator, PH Research, morgan@phresearchoncology.com
Scientific contact	Clinical Trial Coordinator, PH Research, morgan@phresearchoncology.com

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	30 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 January 2019
Global end of trial reached?	Yes
Global end of trial date	25 January 2019
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

1. Determine objective response rate (ORR) per RECIST v1.1 criteria of this regimen
2. Assess the safety of this combination in patients with pancreatic ductal adenocarcinoma (PDAC)
3. Determine overall survival (OS), progression free survival (PFS), and CA19-9 tumor marker response

Protection of trial subjects:

Enoxaparin was administered to all subjects to minimize the risk of thromboembolic events and piroxicam was administered for musculoskeletal symptoms. Prophylactic use of a proton-pump inhibitor (e.g. omeprazole daily or equivalent) was also required for all patients while receiving PEGPH20.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	9 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	5
From 65 to 84 years	3



## Subject disposition

### Recruitment

Recruitment details:

The date of informed consent for the first subject in the study is 12/Jan/2018 and for the last subject in the study is 16/Nov/2018. All patients were recruited in Spain.

### Pre-assignment

Screening details:

- All enrolled subjects are included in the Intent To Treat Population. This population has been used as the primary population for all efficacy analyses.
- All subjects who receive any study medication are included in the Safety Population.

### Period 1

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

### Arms

<b>Arm title</b>	Experimental
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	PHPG20
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mcg/Kg IV infusion over 10-12 minutes. Cycle 1: Days 1, 4, 8, 11, 15, 18; cycle 2 or more: 1Q2W

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

10 mg/Kg over 60 minutes 1Q2W until disease progression, unacceptable toxicity, death, or withdrawal of consent

<b>Number of subjects in period 1</b>	Experimental
Started	8
Treatment administration	7
Completed	7
Not completed	1
Consent withdrawn by subject	1



## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	3	3	
Age continuous			
Units: years			
median	59		
full range (min-max)	43 to 79	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	4	4	
Race			
Units: Subjects			
Caucasian	8	8	
Histologic diagnosis			
Units: Subjects			
Ductal adenocarcinoma	8	8	
TNM and Stage at diagnosis			
T			
Units: Subjects			
T1	1	1	
T2	2	2	
T3	3	3	
T4	2	2	
TNM and Stage at diagnosis			
N			
Units: Subjects			
Nx	2	2	
N0	3	3	
N1	3	3	
TNM and Stage at diagnosis			
M			
Units: Subjects			
Mx	1	1	
M0	6	6	
M1	1	1	
TNM and Stage at diagnosis			
Stage			
Units: Subjects			

0 stage	1	1	
IA	1	1	
IB	1	1	
IIB	2	2	
III	2	2	
IV	1	1	
Current TNM and Stage			
T			
Units: Subjects			
Tx	1	1	
T1	1	1	
T2	2	2	
T3	2	2	
T4	1	1	
UNK	1	1	
Current TNM and Stage			
N			
Units: Subjects			
Nx	1	1	
N0	3	3	
N1	4	4	
Current TNM and Stage			
M			
Units: Subjects			
M1	8	8	
Current TNM and Stage			
Stage			
Units: Subjects			
IV	8	8	
ECOG-PS at baseline			
Units: Subjects			
ECOG-PS 0	3	3	
ECOG-PS 1	5	5	
Previous treatment: radiotherapy			
Units: Subjects			
Yes	2	2	
No	6	6	
Previous treatment: surgery			
Number of surgeries			
Units: Subjects			
Yes	4	4	
No	4	4	
Previous treatments: chemotherapy			
Number of schemes of chemotherapy			
Units: Subjects			
One	1	1	
Two	4	4	
Three	2	2	
Five	1	1	
Number of locations per subject			
Units: Subjects			

One	4	4	
Two	2	2	
Four	1	1	
Five	1	1	
Height Units: cm median full range (min-max)	163.00 150.00 to 180.00	-	
Weight Units: Kg median full range (min-max)	56.75 45.40 to 97.00	-	
Body surface area Units: m2 median full range (min-max)	1.60 1.40 to 2.15	-	
Systolic blood pressure Units: mmHg median full range (min-max)	133.50 103.00 to 140.00	-	
Diastolic blood pressure Units: mmHg median full range (min-max)	79.00 68.00 to 93.00	-	
Heart rate Units: Beats per minute median full range (min-max)	78.50 54.00 to 103.00	-	
Time from first diagnosis to IC Units: months median full range (min-max)	17.40 4.41 to 26.51	-	
Relative dose intensity PEGPH 20 Units: NA median full range (min-max)	0.89 0.50 to 0.99	-	
Relative dose intensity Avelumab Units: NA median full range (min-max)	0.94 0.00 to 1.00	-	

## End points

### End points reporting groups

Reporting group title	Experimental
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Reporting group description: -

### Primary: Best Response (RECIST v1.1)

End point title	Best Response (RECIST v1.1) <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

From start of treatment to end of 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: One arm non-controlled clinical trial. Only descriptive analyses performed. No comparisons.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Patients				
Progression Disease	6			
Stable Disease	1			

### Statistical analyses

No statistical analyses for this end point

### Primary: Overall Survival

End point title	Overall Survival <sup>[2]</sup>
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End point description:

End point type	Primary
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End point timeframe:

From the date of first study treatment administration until the date of the death from any cause.

Notes:

[2] - 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: One arm non-controlled clinical trial. Only descriptive analyses performed. No comparisons.

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: months				
median (confidence interval 95%)				
months	3.29 (2.78 to 3.80)			

### Statistical analyses

No statistical analyses for this end point

### Primary: Progression Free Survival

End point title | Progression Free Survival<sup>[3]</sup>

End point description:

End point type | Primary

End point timeframe:

From the date of first study treatment administration until the date of the RECIST v1.1 progression or death from any cause, whichever occurs first.

Notes:

[3] - 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: One arm non-controlled clinical trial. Only descriptive analyses performed. No comparisons.

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: months				
median (confidence interval 95%)				
months	1.84 (1.76 to 1.93)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Immune Response Progression Free Survival

End point title | Immune Response Progression Free Survival

End point description:

End point type | Secondary

End point timeframe:

From the date of first study treatment administration until the date of the IR-RECIST progression or death from any cause.

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: months				
median (confidence interval 95%)				
months	3.09 (0.48 to 5.71)			

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Number of treatment cycles

End point title	Number of treatment cycles
End point description:	
End point type	Other pre-specified
End point timeframe:	
From first dose of study treatment until end of study treatment	

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: patients				
One	4			
Two	1			
Three	2			

### Statistical analyses

No statistical analyses for this end point

### Post-hoc: Objective response rate

End point title	Objective response rate
End point description:	
End point type	Post-hoc
End point timeframe:	
From start of treatment to end of treatment	

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of patients				
number (confidence interval 95%)				
Objective Response (CR+PR)	0.0 (0.0 to 0.0)			

### Statistical analyses

No statistical analyses for this end point

### Post-hoc: Clinical Benefit rate

End point title	Clinical Benefit rate
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End point description:

End point type	Post-hoc
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End point timeframe:

From start of treatment to end of treatment

<b>End point values</b>	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of patients				
median (confidence interval 95%)				
Clinical benefit (CR + PR + SD)	14.3 (0.0 to 40.2)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment until the end of long term follow-up

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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### Reporting groups

Reporting group title	Total Subjects affected by non-serious adverse events
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Reporting group description: -

<b>Serious adverse events</b>	Total Subjects affected by non-serious adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Confusional state			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Total Subjects affected by non-serious adverse events		
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 7 (100.00%)		
Investigations Blood thyroid stimulating hormone decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Nervous system disorders Muscle contractions involuntary subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)  Feeling cold subjects affected / exposed occurrences (all)  Oedema peripheral	4 / 7 (57.14%) 4  1 / 7 (14.29%) 1		

subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3		
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Eye disorders Eye pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Anal incontinence subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Constipation subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Mesenteric vein thrombosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Nausea subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Vomiting			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Respiratory, thoracic and mediastinal disorders Dysphonia subjects affected / exposed occurrences (all)  Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1  1 / 7 (14.29%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)  Muscle spasms subjects affected / exposed occurrences (all)  Musculoskeletal stiffness subjects affected / exposed occurrences (all)  Myalgia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1  5 / 7 (71.43%) 5  2 / 7 (28.57%) 2  2 / 7 (28.57%) 2		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)  Urinary tract infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1  1 / 7 (14.29%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2018	A serum chemistry has been added at cycle 1, days 4, 11 and 18. New hepatic function test in Cycle 1 all visits and Cycle 2, first visit. Eligibility criteria. Study design has been modified to include a 3+3 scheme.
27 December 2018	Avelumab Investigator Brochure has been updated from 7th to 8th version and data protection regulations were updated to current regulation.

Notes:

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### 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.

Low number of patients included in the study.

Notes: