



Clinical trial results:

A non-controlled, single arm, open label, Phase II study of intravenous and intratumoral administration of ParvOryx in patients with metastatic, inoperable pancreatic cancer

Summary

EudraCT number	2015-001119-11
Trial protocol	DE
Global end of trial date	28 May 2020

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022
Summary attachment (see zip file)	ParvOryxSynopsis_sign (20190229_ParvOryx02_Synopsis_sign.pdf)

Trial information

Trial identification

Sponsor protocol code	ParvOryx02
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02653313
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Oryx GmbH und Co. KG
Sponsor organisation address	Marktplatz 1, Baldham, Germany, 85598
Public contact	Dr. Bernhard Huber (CEO), Oryx GmbH und Co. KG, +49 8106213110, info@oryx-medicine.com
Scientific contact	Dr. Ottheinz Krebs (COO), Oryx GmbH und Co. KG, +49 8106213110, info@oryx-medicine.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	22 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2018
Global end of trial reached?	Yes
Global end of trial date	28 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Primary objectives: To investigate the safety and tolerability of the ParvOryx as well as the associated virus distribution, shedding and elimination
- Secondary objectives: To provide proof of concept for ParvOryx in the treatment of pancreatic cancer assessed by laboratory and clinical characteristics

Protection of trial subjects:

Sequential enrolment

Sequential dose escalation

Safety data were reviewed by a data safety monitoring board (DSMB)

Hospitalisation during and after application of IMP

Background therapy:

In accordance with the European 'Guidance on investigational medicinal products (IMPs) and non investigational medicinal product (NIMPs)', gemcitabine and nab-paclitaxel were defined as non-investigational medicinal products.

Evidence for comparator:

Not applicable (no comparator)

Actual start date of recruitment	17 February 2016
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	Germany: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	6
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited in Germany; 7 patients were treated between 17th February 2016 (first screening examination) and 21st February 2018 (last study visit)

Pre-assignment

Screening details:

Screening phase: Not more than 14 days before the first administration of ParvOryx. Eligible were Patients with stage IV pancreatic ductal adenocarcinoma and at least one hepatic metastasis.

Pre-assignment period milestones

Number of subjects started	7
Number of subjects completed	7

Period 1

Period 1 title	Screening
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose level 1

Arm description:

Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).

Arm type	Experimental
Investigational medicinal product name	ParvOryx
Investigational medicinal product code	
Other name	Parvovirus H1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 1:

- Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 6 x 1E8 pfu (slow infusion)
- Total dose: 1 x 1E9 pfu

Arm title	Dose level 2
------------------	--------------

Arm description:

Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme: Intravenous: 5 E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3 E09 pfu.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	ParvOryx
Investigational medicinal product code	ParvOryx
Other name	Parvovirus H-1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 2:

- Intravenous: 5 E08 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 3 E09 pfu (slow infusion)
- Total dose: 5 E09 pfu

Arm title	Dose level 3
------------------	--------------

Arm description:

Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme: 1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).

Arm type	Experimental
Investigational medicinal product name	ParvOryx
Investigational medicinal product code	ParvOryx
Other name	Parvovirus H-1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 3:

- Intravenous: 1 x 1E9 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 6 x 1E9 pfu (slow infusion)
- Total dose: 1 x 1E10 pfu

Number of subjects in period 1	Dose level 1	Dose level 2	Dose level 3
Started	1	3	3
Completed	1	3	3

Period 2

Period 2 title	Treatment & Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Dose Level 1
Arm description: Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).	
Arm type	Experimental
Investigational medicinal product name	ParvOryx
Investigational medicinal product code	ParvOryx
Other name	Parvovirus H-1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 1:

- Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 6 x 1E8 pfu (slow infusion)
- Total dose: 1 x 1E9 pfu

Arm title	Dose Level 2
Arm description: Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme: Intravenous: 5E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3E09 pfu.	
Arm type	Experimental
Investigational medicinal product name	ParvOryx
Investigational medicinal product code	Parvoryx
Other name	Parvovirus H-1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 2:

- Intravenous: 5 x 1E8 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 3 x 1E9 pfu (slow infusion)
- Total dose: 5 x 1E9 pfu

Arm title	Dose Level 3
Arm description: Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme: 1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).	
Arm type	Experimental
Investigational medicinal product name	ParvOryx
Investigational medicinal product code	ParvOryx
Other name	Parvovirus H-1 in Visipaque/Ringer solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use, Intravenous use

Dosage and administration details:

Dose level 3:

- Intravenous: 1 x 1E9 pfu (2-hour infusion) per day over 4 days
- Intratumoral: 6 x 1E9 pfu (slow infusion)
- Total dose: 1 x 1E10 pfu

Number of subjects in period 2	Dose Level 1	Dose Level 2	Dose Level 3
Started	1	3	3
Completed	1	3	3

Baseline characteristics

Reporting groups

Reporting group title	Screening
-----------------------	-----------

Reporting group description:

All patients enrolled are reported regarding baseline characteristics

Reporting group values	Screening	Total	
Number of subjects	7	7	
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)	6	6	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous			
Age (full analysis set)			
Units: years			
arithmetic mean	55.1		
standard deviation	± 10.6	-	
Gender categorical			
Units: Subjects			
Female	3	3	
Male	4	4	

Subject analysis sets

Subject analysis set title	Full analysis set/Safety set
----------------------------	------------------------------

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

Full Analysis Set (FAS): Consists of those subjects who were included in the trial and received the study medication at least once. The term "Intention-to-treat analysis" (ITT analysis) is used for an analysis applying the ITT principle to all subjects of the FAS. This means that all subjects are analysed as if they had been treated as specified in the study protocol.

In this study, the safety set is identical to the FAS.

Subject analysis set title	Dose level 1
----------------------------	--------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).

Subject analysis set title	Dose level 2
----------------------------	--------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme:
Intravenous: 5 E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3 E09 pfu.

Subject analysis set title	Dose Level 3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme:
1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).

Reporting group values	Full analysis set/Safety set	Dose level 1	Dose level 2
Number of subjects	7	1	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)	6	1	3
From 65-84 years	1	0	0
85 years and over	0	0	0
Age continuous			
Age (full analysis set)			
Units: years			
arithmetic mean	55.1		
standard deviation	± 10.6	±	±
Gender categorical Units: Subjects			
Female	3		
Male	4		

Reporting group values	Dose Level 3		
Number of subjects	3		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	2		
From 65-84 years	1		
85 years and over	0		

Age continuous			
Age (full analysis set)			
Units: years arithmetic mean standard deviation	\pm		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Dose level 1
-----------------------	--------------

Reporting group description:

Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).

Reporting group title	Dose level 2
-----------------------	--------------

Reporting group description:

Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme: Intravenous: 5 E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3 E09 pfu.

Reporting group title	Dose level 3
-----------------------	--------------

Reporting group description:

Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme: 1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).

Reporting group title	Dose Level 1
-----------------------	--------------

Reporting group description:

Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).

Reporting group title	Dose Level 2
-----------------------	--------------

Reporting group description:

Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme: Intravenous: 5E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3E09 pfu.

Reporting group title	Dose Level 3
-----------------------	--------------

Reporting group description:

Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme: 1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).

Subject analysis set title	Full analysis set/Safety set
----------------------------	------------------------------

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

Full Analysis Set (FAS): Consists of those subjects who were included in the trial and received the study medication at least once. The term "Intention-to-treat analysis" (ITT analysis) is used for an analysis applying the ITT principle to all subjects of the FAS. This means that all subjects are analysed as if they had been treated as specified in the study protocol.

In this study, the safety set is identical to the FAS.

Subject analysis set title	Dose level 1
----------------------------	--------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Administration of IMP at the total dose of 1E09 pfu. The total dose was applied by the following scheme: Intravenous: 1 x 1E8 pfu (2-hour infusion) per day over 4 days, intratumorally: 6 x 1E8 pfu (slow infusion).

Subject analysis set title	Dose level 2
----------------------------	--------------

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

Administration of IMP at the total dose 5E09 pfu. The total dose was applied by the following scheme: Intravenous: 5 E08 pfu (2-hour infusion) per day over 4 days, and an intratumoral slow infusion of 3 E09 pfu.

Subject analysis set title	Dose Level 3
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Administration of IMP at a total dose of 1E10 pfu. The total dose was applied by the following scheme: 1 x 1E9 pfu intravenous (2-hour infusion) per day over 4 days and Intratumoral: 6 x 1E9 pfu (administered in one slow infusion).	

Primary: Safety and tolerability of ParvOryx

End point title	Safety and tolerability of ParvOryx ^[1]
End point description:	
Treatment with ParvOryx is considered as safe and well-tolerated if none of the following events occurs:	
<ul style="list-style-type: none"> • Elevation of ALAT, ASAT, alkaline phosphatase, or bilirubin > 3 times of the baseline value up to Day 28, • CRP > 3 times of the baseline value up to Day 28, • Neutrophiles < 1.0 x 1E09/L or > 12.0 x 1E09/L up to Day 28, • Hemoglobin < 7.5 g/L up to Day 28, • Thrombocytes < 50 x 1E09/L • INR > 2.5 or aPTT > 50 sec. up to Day 28, • Neurological symptoms with no other explanation than administration of ParvOryx (e.g. brain metastasis) up to Day 28, • Thromboembolic event(s), myocardial infarction or stroke • Deteriorations in medical parameters, which were classified as at least 'possibly' related to the IMP and required countermeasures to avert conditions fulfilling at least one of the 'seriousness'-criteria, throughout the trial. • SAE(s) classified as at least 'possibly' related to the IMP throughout the trial • medical necessity to interrupt or terminate treatment 	
End point type	Primary
End point timeframe:	
during treatment phase and follow-up	
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: Descriptive statistics only	

End point values	Dose Level 1	Dose Level 2	Dose Level 3	Full analysis set/Safety set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1	3	3	7
Units: number of patients who tolerated IMP	1	2	2	5

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-Free Survival

End point title	Median Progression-Free Survival
End point description:	
End point type	Secondary
End point timeframe:	
The complete trial	

End point values	Full analysis set/Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: days	72			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Overall Survival

End point title	Median Overall Survival
End point description:	
End point type	Secondary
End point timeframe: throughout the trial	

End point values	Full analysis set/Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: days	176			

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events

End point title	Adverse Events
End point description:	
End point type	Secondary
End point timeframe: Throughout the trial	

End point values	Dose Level 1	Dose Level 2	Dose Level 3	Full analysis set/Safety set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1	3	3	7
Units: Events	15	49	31	95

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:
throughout the trial

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	18.1
--------------------	------

Reporting groups

Reporting group title	Dose Level 1
-----------------------	--------------

Reporting group description: -

Reporting group title	Dose Level 2
-----------------------	--------------

Reporting group description: -

Reporting group title	Dose Level 3
-----------------------	--------------

Reporting group description: -

Serious adverse events	Dose Level 1	Dose Level 2	Dose Level 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
number of deaths (all causes)	1	3	2
number of deaths resulting from adverse events	0	0	0
Investigations			
Hypercalcaemia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dose Level 1	Dose Level 2	Dose Level 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 1 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
occurrences (all)	0	2	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2015	This amendment (approved by the PEI not needed; by the EC on 29th September 2015) concerned additional requirement made by the PEI. This amendment led to protocol version 5.
24 February 2016	This amendment (approved by the EC on 24th February 2016 and by the PEI on 26th February 2016) concerned the implementation of MRI as the basis for assessment of clinical response (additional assessment on the days of intratumoral administration and on Day 28). In addition, an Information sheet for patients' relatives was provided for approval to the EC. This amendment led to protocol version 6.
15 July 2016	This amendment (approved by the PEI on 15th July 2016 and by the EC on 21st June 2016) concerned exclusion criterion no. 3: "peritoneal carcinosis" was augmented with "clinically apparent ascites", and some other, formal, changes were made. This amendment led to protocol version 7.
25 October 2016	This amendment (approved by the PEI on 3rd November 2016 and by the EC on 25th October 2016) concerned the annual up-date of the IB only. This amendment affected the IB only.
14 December 2016	This amendment (approved by the PEI not needed; by the EC on 14th December 2016) concerned a change of personnel; a second deputy of the principal investigator changed (formerly Dr. Athanasios Mavratzas, then Dr. Nicolas Hohmann) and information about prolongation of trial duration. (See Appendix 16.1.1.7.) This was an administrative amendment and did not require a new protocol version.
03 January 2017	This amendment (approved by the PEI on 20th January 2017 and by the EC on 3rd January 2107) allowed the parallel inclusion of patients nos. 4 and 5 and of patients nos. 6 and 7. This amendment led to protocol version 8.
26 September 2017	This amendment (approved by the PEI on 10th October 2017 and by the EC on 26th September 2017) concerned the annual up-date of the IB only. This amendment affected the IB only.
10 April 2018	This amendment (approved by the PEI on 23rd April 2018 and by the EC on 10th April 2018) introduced the replacement of all patients who did not receive the complete course of study treatment. This amendment led to protocol version 9.

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.

not applicable

Notes: