



Clinical trial results:

A Single-arm, Multi-Center, Open-Label Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Melphalan/HDS Treatment in Patients with Hepatic-Dominant Ocular Melanoma.

Summary

EudraCT number	2015-000417-44
Trial protocol	GB DE AT BE ES IT
Global end of trial date	30 August 2023

Results information

Result version number	v1 (current)
This version publication date	05 July 2025
First version publication date	05 July 2025

Trial information

Trial identification

Sponsor protocol code	PHP-OCM-301A
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Delcath Systems, Inc.
Sponsor organisation address	1633 Broadway 22nd Floor, Suite C, New York, United States, 10019
Public contact	Clinical Trials Desk, Delcath Systems, Inc, +1 2124892100, jshea@delcath.com
Scientific contact	Clinical Trials Desk, Delcath Systems, Inc, +1 2124892100, jshea@delcath.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	02 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate objective response rate (ORR) (complete response + partial response) as determined by Independent Central Review Committee (IRC).

Protection of trial subjects:

This study was designed and monitored in accordance with sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 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	European Union: 46
Country: Number of subjects enrolled	United States: 49
Worldwide total number of subjects	95
EEA total number of subjects	0

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)	65
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 23 centers in the US and Europe. Initially, Protocol PHP-OCM-301 (Protocol 301) was a randomized, 2-arm study including a treatment group of Melphalan/HDS and a control group of best alternative care (BAC), the protocol was amended to be an open-label, single-arm study PHP-OCM-301A (Protocol 301A).

Pre-assignment

Screening details:

Of the total subjects enrolled in the pooled 301/301A group all received treatment with Melphalan/HDS. Male or female subjects ≥ 18 years of age having 50% or less histologically or cytologically proven ocular melanoma (OM) metastases in the parenchyma of the liver.

Period 1

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

Arms

Arm title	Pooled 301/301A
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Arm description:

The enrolled subjects received melphalan/HDS at a dose of 3.0 mg/kg ideal body weight.

Arm type	Experimental
Investigational medicinal product name	Melphalan hydrochloride for injection/Hepatic Delivery System (Melphalan/HDS)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Melphalan at a dose of 3.0 mg/Kg ideal body weight was administered once every 6 weeks for a total of 6 cycles.

Number of subjects in period 1 ^[1]	Pooled 301/301A
Started	91
Completed	34
Not completed	57
Adverse event, serious fatal	11
Consent withdrawn by subject	3
Investigator's decision	9
Adverse event, non-fatal	6
COVID-19	1
Overall disease progression need systemic therapy	8
Hepatic-only disease progression	3

Overall disease progression- investigator decisio	15
Poor subject compliance	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: In this study, efficacy analyses were performed in 91 subjects who received study treatment (Treated population), while safety analyses were performed in 95 subjects. Treatment was attempted for the 4 additional subjects in the Safety Population, but the drug was not delivered.

Baseline characteristics

Reporting groups

Reporting group title	Pooled 301/301A
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Reporting group description:

The enrolled subjects received melphalan/HDS at a dose of 3.0 mg/kg ideal body weight.

Reporting group values	Pooled 301/301A	Total	
Number of subjects	91	91	
Age categorical			
Units: Subjects			
Adults (18-64 years)	61	61	
From 65-84 years	30	30	
Age continuous			
Units: years			
arithmetic mean	57.7		
standard deviation	± 11.62	-	
Gender categorical			
Units: Subjects			
Female	47	47	
Male	44	44	
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	2	
Non-Hispanic or Latino	86	86	
No response	3	3	
Race			
Units: Subjects			
White	86	86	
Other	2	2	
No response	3	3	
Baseline Extent of Liver Involvement			
Hepatic tumor burden per IRC was the sum of target hepatic lesion diameters (in millimeters). Extent of liver involvement was assessed by the Investigator.			
Units: Subjects			
1% to 25%	72	72	
26% to 50%	19	19	
Number of Hepatic Lesions			
Based on IRC assessment of lesions using RECIST v1.1.			
Units: Subjects			
n=1	4	4	
n=2	19	19	
n=3	67	67	
n=4	1	1	
n=5 or more	0	0	
Any Extrahepatic Lesion			
Based on IRC assessment of lesions using RECIST v1.1.			
Units: Subjects			
No	64	64	

Yes	27	27	
Number of Extrahepatic Lesions			
Based on IRC assessment of lesions using RECIST v1.1.			
Units: Subjects			
n=0	64	64	
n=1	18	18	
n=2 or more	9	9	
Baseline Eastern Cooperative Oncology Group (ECOG) Performance Status			
Units: Subjects			
0=asymptomatic	80	80	
1=symptomatic, completely ambulatory	9	9	
2=symptomatic, <50% bed rest	0	0	
3=symptomatic, ≥50% bed rest	0	0	
4=bed bound	0	0	
Unknown	2	2	
Height			
The data for this baseline characteristic (height) is available for 90 subjects.			
Units: cm			
arithmetic mean	170.27		
standard deviation	± 9.774	-	
Weight			
Units: Kg			
arithmetic mean	79.40		
standard deviation	± 21.144	-	
Months Since Diagnosis of Primary Tumor			
Months from diagnosis of either primary tumor or liver metastases to either randomization (Study 301) or eligibility (Study 301A).			
Units: Months			
arithmetic mean	48.94		
standard deviation	± 38.513	-	
Months Since Diagnosis of Liver Metastases			
Months from diagnosis of either primary tumor or liver metastases to either randomization (Study 301) or eligibility (Study 301A).			
Units: Months			
arithmetic mean	9.58		
standard deviation	± 12.196	-	
Months From Primary Diagnosis to Metastasis to the Liver			
Units: Months			
arithmetic mean	39.36		
standard deviation	± 32.844	-	
Baseline Hepatic Tumor Burden			
Hepatic tumor burden per IRC was the sum of target hepatic lesion diameters (in millimeters). Extent of liver involvement was assessed by the Investigator. The data for this baseline characteristic (baseline hepatic tumor burden) is available for 90 subjects.			
Units: mm			
arithmetic mean	57.77		
standard deviation	± 30.430	-	
Aspartate aminotransferase			
The data for this baseline characteristic (aspartate aminotransferase) is available for 90 subjects.			

Units: U/L			
arithmetic mean	30.0		
standard deviation	± 14.74	-	
Alanine aminotransferase			
The data for this baseline characteristic (alanine aminotransferase) is available for 90 subjects.			
Units: U/L			
arithmetic mean	33.9		
standard deviation	± 23.10	-	
Alkaline phosphatase			
Units: U/L			
arithmetic mean	97.2		
standard deviation	± 51.77	-	
Bilirubin			
The data for this baseline characteristic (bilirubin) is available for 89 subjects.			
Units: µmol/L			
arithmetic mean	9.5		
standard deviation	± 5.00	-	
Direct bilirubin			
The data for this baseline characteristic (direct bilirubin) is available for 62 subjects.			
Units: µmol/L			
arithmetic mean	3.2		
standard deviation	± 1.60	-	
Albumin			
The data for this baseline characteristic (albumin) is available for 88 subjects.			
Units: g/L			
arithmetic mean	42.7		
standard deviation	± 4.12	-	
Lactate dehydrogenase			
The data for this baseline characteristic (lactate dehydrogenase) is available for 86 subjects.			
Units: U/L			
arithmetic mean	316.9		
standard deviation	± 248.17	-	

End points

End points reporting groups

Reporting group title	Pooled 301/301A
Reporting group description:	
The enrolled subjects received melphalan/HDS at a dose of 3.0 mg/kg ideal body weight.	

Primary: Percentage of Subjects Achieving Objective Response Rate (ORR)

End point title	Percentage of Subjects Achieving Objective Response Rate (ORR) ^[1]
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End point description:

An objective response (OR) is defined as a best overall response (BOR) of complete response (CR) or partial response (PR). Objective response rate (ORR) is the proportion of subjects with an objective response by IRC using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria. CR: Disappearance of all target lesions, any pathological lymph nodes (target or non-target) must be <10 mm in short axis diameter. PR: ≥30% decrease in the sum of the long axis diameters of the target lesions, using the baseline sum as reference. The treated population included all subjects treated with Melphalan/HDS.

End point type	Primary
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End point timeframe:

At Week 6 (or the Last Week of the Cycle)

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: No statistical analyses for this end point because this is a single arm study.

End point values	Pooled 301/301A			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: percent				
number (confidence interval 95%)	36.3 (26.44 to 47.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) as Determined by IRC

End point title	Duration of response (DOR) as Determined by IRC
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End point description:

Duration of response (DOR) was defined as the time from the 1st documented confirmed response of CR or PR based on RECIST v1.1 determined by the IRC and the investigator to the 1st documented progression of liver metastatic disease or death due to any cause. The treated population included all subjects treated with Melphalan/HDS. The number of subjects analyzed is the subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

At Week 6 (or the Last Week of the Cycle)

End point values	Pooled 301/301A			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Months				
median (confidence interval 95%)	14.00 (8.31 to 17.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Disease Control Rate (DCR) as Determined by IRC

End point title	Percentage of Subjects Achieving Disease Control Rate (DCR) as Determined by IRC
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End point description:

Disease control was defined as a best overall response of CR, PR, or stable disease (SD). DCR was the proportion of subjects with an objective response of CR of any duration, PR of any duration, or SD for a minimum of 12 weeks from the eligibility date as determined by IRC and the investigator based on RECIST v1.1. The treated population included all subjects treated with Melphalan/HDS.

End point type	Secondary
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End point timeframe:

At Week 6 (or the Last Week of the Cycle)

End point values	Pooled 301/301A			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Percent				
number (confidence interval 95%)	73.6 (63.35 to 82.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

Overall survival (OS) is defined as the time from the eligibility date to date of death due to any cause. The treated population included all subjects treated with Melphalan/HDS.

End point type	Secondary
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End point timeframe:

As of the clinical data cut-off of 02 December 2022.

End point values	Pooled 301/301A			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Months				
median (confidence interval 95%)	20.53 (16.79 to 25.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) as Determined by IRC

End point title	Progression Free Survival (PFS) as Determined by IRC
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End point description:

Progression free survival (PFS) was defined as the time from the eligibility date to the 1st documented progression or death due to any cause determined by the IRC and the investigator. The treated population included all subjects treated with Melphalan/HDS.

End point type	Secondary
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End point timeframe:

Till the End of Study (EOS)

End point values	Pooled 301/301A			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Months				
median (confidence interval 95%)	9.03 (6.34 to 11.56)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to follow-up period (until death)

Adverse event reporting additional description:

The Safety population (n=95) included all treated subjects with Melphalan/HDS (n=91), and the population in which treatment was attempted (n=4) reported TEAEs. TEAEs observed in all subjects have been listed for non-serious adverse events.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Pooled 301/301A
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Reporting group description:

The enrolled subjects received melphalan/HDS at a dose of 3.0 mg/kg ideal body weight.

Serious adverse events	Pooled 301/301A		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 95 (45.26%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 95 (2.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	2 / 95 (2.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	2 / 95 (2.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	2 / 95 (2.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemothorax			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Platelet count decreased			
subjects affected / exposed	6 / 95 (6.32%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	2 / 95 (2.11%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
International normalised ratio increased			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Troponin T increased			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			

subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	3 / 95 (3.16%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Arrhythmia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bundle branch block right			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cyanosis			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cerebral infarction			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	9 / 95 (9.47%)		
occurrences causally related to treatment / all	8 / 9		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences causally related to treatment / all	8 / 8		
deaths causally related to treatment / all	0 / 0		
Leukopenia			

subjects affected / exposed	4 / 95 (4.21%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal tenderness			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cholecystitis acute			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hepatic artery thrombosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 0 / 1 0 / 0		
Hepatic failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 1 / 1 0 / 0		
Hepatitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 1 / 1 0 / 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 0 / 1 0 / 0		
Groin pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 0 / 1 0 / 0		
Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 0 / 1 0 / 0		
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 0 / 1 0 / 0		
Neutropenic sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 95 (1.05%) 1 / 1 0 / 0		

Peritonitis bacterial			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 95 (1.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pooled 301/301A		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 95 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	11 / 95 (11.58%)		
occurrences (all)	11		
Hypertension			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	51 / 95 (53.68%)		
occurrences (all)	51		
Pyrexia			
subjects affected / exposed	15 / 95 (15.79%)		
occurrences (all)	15		
Asthenia			

subjects affected / exposed	12 / 95 (12.63%)		
occurrences (all)	12		
Catheter site bruise			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	6 / 95 (6.32%)		
occurrences (all)	6		
Pain			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Catheter site pain			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Chills			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	22 / 95 (23.16%)		
occurrences (all)	25		
Cough			
subjects affected / exposed	14 / 95 (14.74%)		
occurrences (all)	14		
Oropharyngeal pain			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Pulmonary oedema			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Investigations			

Platelet count decreased			
subjects affected / exposed	42 / 95 (44.21%)		
occurrences (all)	42		
Alanine aminotransferase increased			
subjects affected / exposed	30 / 95 (31.58%)		
occurrences (all)	32		
International normalised ratio increased			
subjects affected / exposed	29 / 95 (30.53%)		
occurrences (all)	29		
Activated partial thromboplastin time prolonged			
subjects affected / exposed	27 / 95 (28.42%)		
occurrences (all)	27		
Aspartate aminotransferase increased			
subjects affected / exposed	27 / 95 (28.42%)		
occurrences (all)	27		
Blood alkaline phosphatase increased			
subjects affected / exposed	26 / 95 (27.37%)		
occurrences (all)	31		
White blood cell count decreased			
subjects affected / exposed	21 / 95 (22.11%)		
occurrences (all)	21		
Lymphocyte count decreased			
subjects affected / exposed	12 / 95 (12.63%)		
occurrences (all)	12		
Troponin I increased			
subjects affected / exposed	12 / 95 (12.63%)		
occurrences (all)	12		
Blood bilirubin increased			
subjects affected / exposed	10 / 95 (10.53%)		
occurrences (all)	10		
Neutrophil count decreased			
subjects affected / exposed	9 / 95 (9.47%)		
occurrences (all)	9		
Haemoglobin decreased			

subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Troponin T increased			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Troponin increased			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Blood albumin decreased			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Electrocardiogram QT prolonged			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Gamma-glutamyltransferase increased			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Blood calcium decreased			
subjects affected / exposed	6 / 95 (6.32%)		
occurrences (all)	6		
Blood glucose increased			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	6		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	16 / 95 (16.84%)		
occurrences (all)	16		
Post procedural haemorrhage			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Procedural nausea			

subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	5 / 95 (5.26%) 5 5 / 95 (5.26%) 5		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	5 / 95 (5.26%) 5		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all)	18 / 95 (18.95%) 18 11 / 95 (11.58%) 11 8 / 95 (8.42%) 10 7 / 95 (7.37%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Febrile neutropenia	55 / 95 (57.89%) 58 28 / 95 (29.47%) 28 25 / 95 (26.32%) 25 20 / 95 (21.05%) 20 Febrile neutropenia		

subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Lymphopenia			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	54 / 95 (56.84%)		
occurrences (all)	56		
Vomiting			
subjects affected / exposed	33 / 95 (34.74%)		
occurrences (all)	34		
Abdominal pain upper			
subjects affected / exposed	21 / 95 (22.11%)		
occurrences (all)	22		
Abdominal pain			
subjects affected / exposed	16 / 95 (16.84%)		
occurrences (all)	16		
Diarrhoea			
subjects affected / exposed	15 / 95 (15.79%)		
occurrences (all)	15		
Abdominal distension			
subjects affected / exposed	8 / 95 (8.42%)		
occurrences (all)	8		
Constipation			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Dyspepsia			
subjects affected / exposed	7 / 95 (7.37%)		
occurrences (all)	7		
Abdominal discomfort			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	5 / 95 (5.26%)		
occurrences (all)	5		

<p>Skin and subcutaneous tissue disorders</p> <p>Alopecia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ecchymosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 95 (6.32%)</p> <p>6</p> <p>6 / 95 (6.32%)</p> <p>6</p> <p>6 / 95 (6.32%)</p> <p>6</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Groin pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscular weakness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Musculoskeletal chest pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Musculoskeletal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>25 / 95 (26.32%)</p> <p>25</p> <p>10 / 95 (10.53%)</p> <p>10</p> <p>10 / 95 (10.53%)</p> <p>10</p> <p>9 / 95 (9.47%)</p> <p>9</p> <p>5 / 95 (5.26%)</p> <p>5</p> <p>5 / 95 (5.26%)</p> <p>5</p> <p>5 / 95 (5.26%)</p> <p>6</p> <p>5 / 95 (5.26%)</p> <p>5</p>		
<p>Metabolism and nutrition disorders</p>			

Decreased appetite subjects affected / exposed occurrences (all)	15 / 95 (15.79%) 15		
Hypocalcaemia subjects affected / exposed occurrences (all)	12 / 95 (12.63%) 12		
Hypokalaemia subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 9		
Hypomagnesaemia subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 9		
Hypophosphataemia subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 9		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	8 / 95 (8.42%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2015	Change in the language of the secondary objectives, inclusion criteria. In statistical analysis section, detailed information was added for efficacy outcomes Progression-free survival (PFS) [as determined by Independent Central Review] and Objective Response Rate [as determined by Independent Central Review]
20 April 2016	Change in exclusion criteria was made (Patients previously treated with any intra-arterial regional hepatic therapy; this exclusion criteria was deleted) Additional criteria were added for Patient Withdrawal from Treatment
18 January 2017	Changes were made in the exclusion criteria for the Sexually active females of childbearing potential and sexually active males with partners of reproductive potential; information regarding Pearl Index < 1% was added New exclusion criteria "Patients who have been institutionalized by governmental or legal decree or who are employees of the sponsor, Investigator, or study site." was added Information was updated related to prohibited medications
04 December 2017	Language-related changes were introduced in the inclusion/exclusion criteria, study design, Dosing and Dose Modification, PD-1 Inhibitors Safety, Imaging, Device and Procedural Assessment sections.
22 June 2018	Open-label, single-arm study in up to 80 patients with ocular melanoma (30 patients already enrolled on PHP-OCM-301 and an additional 50 patients to be enrolled on PHP-OCM-301A). Primary endpoint is ORR based on Independent Central Review Committee. For CR or PR, tumor measurements shall be confirmed by repeat assessments ≥ 4 weeks after initial documentation. Secondary endpoints are Duration of Response (DOR) as determined by IRC, Disease Control Rate (DCR) as determined by IRC, overall survival, and PFS as determined by IRC.

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.

None reported

Notes: