

**Clinical trial results:****A RANDOMIZED CONTROLLED STUDY ON THE EFFECTIVENESS OF FIRST-LINE CHEMOTHERAPY (CARBOPLATIN AND PACLITAXEL) VERSUS CHEMO-IMMUNOTHERAPY (CARBOPLATIN-PACLITAXEL-OREGOVOMAB) IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN, ADNEXAL OR PERITONEAL CARCINOMA****Summary**

EudraCT number	2010-024305-13
Trial protocol	IT
Global end of trial date	12 October 2018

Results information

Result version number	v1 (current)
This version publication date	16 October 2021
First version publication date	16 October 2021

Trial information**Trial identification**

Sponsor protocol code	QPT-ORE-02
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01616303
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OncoQuest Pharmaceuticals Inc.
Sponsor organisation address	670-21 Sannae-ro, Sannae-myeon Miryang-Si, Korea, Republic of,
Public contact	Thomas Woo, VP of Product Development, OncoQuest Pharmaceuticals Inc., 1 780 448 1400, thomas@oncoquestinc.com
Scientific contact	Thomas Woo, VP of Product Development, OncoQuest Pharmaceuticals Inc., 1 780 448 1400, thomas@oncoquestinc.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	21 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2015
Global end of trial reached?	Yes
Global end of trial date	12 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Confirm and clarify the preliminary results of Braly8 on the induction of CA125-specific cellular immunity of clinical relevance with Oregovomab infusion associated with first-line chemotherapy in patients with stage III-IV ovarian cancer. The primary objective of the clinical trial is the evaluation of anti CA125 cellular immune response by ELISPOT assay.

Protection of trial subjects:

Each enrolled patient was carefully monitored for any potential adverse events from the study treatment. If any adverse events were happened, patients were treated accordingly. Insurance was also provided.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 81
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	97
EEA total number of subjects	81

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)	72
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 137 patients were screened, and 40 failed screening. A total of 97 patients were randomly assigned to treatment, and 94 were treated; 91 patients entered follow-up. Eight patients (17.0%) in Arm 1 and 12 patients (24.0%) in Arm 2 discontinued from the study.

Pre-assignment

Screening details:

Patients were screened for eligibility up to 4 weeks before treatment. Informed consent was obtained before any protocol-specific screening evaluations were done. Once all eligibility criteria were met, the patient was randomly assigned to a treatment arm. The treatment period began immediately after randomization.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Arm 1

Arm description:

Treatment Arm 1 (40 patients planned) received, sequentially on the same day, carboplatin area under the curve (AUC) 6 administered intravenously (IV) every 3 weeks (21 days) for 6 cycles, paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles, and oregovomab 2 mg infused IV over 20 minutes administered during the first, third, and fifth cycles. Patients in Arm 1 also received oregovomab as monotherapy 12 weeks after the fifth cycle. At the discretion of the investigator, treatment with oregovomab may have been discontinued for patients who experienced an allergic event. No other oregovomab dosage modification was permitted without prior approval from the medical monitor.

Oregovomab, when dosed at 2 mg, has been demonstrated to induce cross-presentation of CA125 peptide fragments and induce a CA125-specific cellular immune response and has been well tolerated in clinical trials.

Arm type	Experimental
Investigational medicinal product name	Oregovomab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Oregovomab was supplied in vials containing 2 mg of the monoclonal antibody with a reducing agent, a buffer complex, and excipients.

The lyophilized contents of the vial of oregovomab were dissolved in 2 mL of 0.9% sodium chloride injection US Pharmacopeia then added to 50 mL of 0.9% sodium chloride injection USP in a small (50 mL) infusion bag.

Paclitaxel was diluted before infusion in 0.9% sodium chloride injection, 5% dextrose injection, 5% dextrose and 0.9% sodium chloride injection, or 5% dextrose in Ringer's injection to a final concentration of 0.3 to 1.2 mg/mL.

Carboplatin powder was reconstituted for injection with sterile water for injection, dextrose 5% in water, or sodium chloride 0.9 concentration of 10 mg/mL. Reconstituted solution, or premixed aqueous solution, may have been further diluted with dextrose 5% in water or sodium chloride 0.9% injection.

Investigational medicinal product name	carboplatin + paclitaxel
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel was diluted before infusion in 0.9% sodium chloride injection, 5% dextrose injection, 5% dextrose and 0.9% sodium chloride injection, or 5% dextrose in Ringer's injection to a final concentration of 0.3 to 1.2 mg/mL.

Carboplatin powder was reconstituted for injection with sterile water for injection, dextrose 5% in water, or sodium chloride 0.9% injection. Diluent was added to produce a solution with a final concentration of 10 mg/mL. Reconstituted solution, or premixed aqueous solution, may have been further diluted with dextrose 5% in water or sodium chloride 0.9% injection

Arm title	Treatment Arm 2
------------------	-----------------

Arm description:

Treatment Arm 2 (40 patients planned) received, sequentially, carboplatin AUC 6 administered IV every 3 weeks (21 days) for 6 cycles, followed by paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles.

Arm type	Active comparator
Investigational medicinal product name	carboplatin + paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel was diluted before infusion in 0.9% sodium chloride injection, 5% dextrose injection, 5% dextrose and 0.9% sodium chloride injection, or 5% dextrose in Ringer's injection to a final concentration of 0.3 to 1.2 mg/mL.

Carboplatin powder was reconstituted for injection with sterile water for injection, dextrose 5% in water, or sodium chloride 0.9 concentration of 10 mg/mL. Reconstituted solution, or premixed aqueous solution, may have been further diluted with dextrose 5% in water or sodium chloride 0.9% injection.

Number of subjects in period 1	Treatment Arm 1	Treatment Arm 2
Started	47	50
Completed	39	38
Not completed	8	12
Consent withdrawn by subject	4	3
death	1	2
Adverse event, non-fatal	2	2
Patient noncompliance	1	2
none	-	2
Medical condition	-	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment Arm 1
-----------------------	-----------------

Reporting group description:

Treatment Arm 1 (40 patients planned) received, sequentially on the same day, carboplatin area under the curve (AUC) 6 administered intravenously (IV) every 3 weeks (21 days) for 6 cycles, paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles, and oregovomab 2 mg infused IV over 20 minutes administered during the first, third, and fifth cycles. Patients in Arm 1 also received oregovomab as monotherapy 12 weeks after the fifth cycle. At the discretion of the investigator, treatment with oregovomab may have been discontinued for patients who experienced an allergic event. No other oregovomab dosage modification was permitted without prior approval from the medical monitor.

Oregovomab, when dosed at 2 mg, has been demonstrated to induce cross-presentation of CA125 peptide fragments and induce a CA125-specific cellular immune response and has been well tolerated in clinical trials.

Reporting group title	Treatment Arm 2
-----------------------	-----------------

Reporting group description:

Treatment Arm 2 (40 patients planned) received, sequentially, carboplatin AUC 6 administered IV every 3 weeks (21 days) for 6 cycles, followed by paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles.

Reporting group values	Treatment Arm 1	Treatment Arm 2	Total
Number of subjects	47	50	97
Age categorical			
The mean and median age of patients in the study was 57.5 and 57.0 years, respectively.			
Units: Subjects			
Adults (18-64 years)	35	37	72
From 65-84 years	12	13	25
Age continuous			
Units: years			
median	58	57	
full range (min-max)	37 to 78	38 to 75	-
Gender categorical			
Units: Subjects			
Female	47	50	97
Male	0	0	0
Race			
Units: Subjects			
African	0	1	1
White	47	49	96
Asian	0	0	0
Other	0	0	0
Country			
Units: Subjects			
USA	8	8	16
Italy	39	42	81

End points

End points reporting groups

Reporting group title	Treatment Arm 1
-----------------------	-----------------

Reporting group description:

Treatment Arm 1 (40 patients planned) received, sequentially on the same day, carboplatin area under the curve (AUC) 6 administered intravenously (IV) every 3 weeks (21 days) for 6 cycles, paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles, and oregovomab 2 mg infused IV over 20 minutes administered during the first, third, and fifth cycles. Patients in Arm 1 also received oregovomab as monotherapy 12 weeks after the fifth cycle. At the discretion of the investigator, treatment with oregovomab may have been discontinued for patients who experienced an allergic event. No other oregovomab dosage modification was permitted without prior approval from the medical monitor.

Oregovomab, when dosed at 2 mg, has been demonstrated to induce cross-presentation of CA125 peptide fragments and induce a CA125-specific cellular immune response and has been well tolerated in clinical trials.

Reporting group title	Treatment Arm 2
-----------------------	-----------------

Reporting group description:

Treatment Arm 2 (40 patients planned) received, sequentially, carboplatin AUC 6 administered IV every 3 weeks (21 days) for 6 cycles, followed by paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles.

Primary: Comparison of CA 125 cellular immune response

End point title	Comparison of CA 125 cellular immune response
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

28 weeks

End point values	Treatment Arm 1	Treatment Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	29		
Units: percentage				
number (not applicable)	34	29		

Statistical analyses

Statistical analysis title	Statistical Analysis Plan (SAP)
----------------------------	---------------------------------

Statistical analysis description:

For qualitative variables, the chi-square test was applied. For continuous variables, the Student's t-test or Wilcoxon-Mann-Whitney test (according to normality of the data) was applied. In both cases, the H₀ (null hypothesis) was that there were no differences between groups for a determinate variable. The level of significance was $\alpha = 0.05$.

All descriptive statistical analyses were performed using SAS version 9.4 or later, unless otherwise noted.

Comparison groups	Treatment Arm 1 v Treatment Arm 2
-------------------	-----------------------------------

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared
Parameter estimate	percentage

Adverse events

Adverse events information

Timeframe for reporting adverse events:

22 December 2011 to 27 December 2017

Adverse event reporting additional description:

Monitoring for adverse experiences was conducted by the investigator throughout the study and the results recorded on the AE Report Form. The investigator graded all adverse experiences as to their severity according to the WHO Toxicity Guidelines. All patients followed for AE/SAE for 30 days following the last dose or until the date of treatment exit

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

Dictionary used

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

Dictionary version	19.0
--------------------	------

Reporting groups

Reporting group title	Treatment Group
-----------------------	-----------------

Reporting group description:

Arm 1: Oregovomab in combination with first-line chemotherapy (carboplatin and paclitaxel) in patients with advanced epithelial ovarian, adnexal, or peritoneal carcinoma.

Arm 1 (40 patients planned) received, sequentially on the same day, carboplatin area under the curve (AUC) 6 administered intravenously (IV) every 3 weeks (21 days) for 6 cycles, paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles, and oregovomab 2 mg infused IV over 20 minutes administered during the first, third, and fifth cycles. Patients in Arm 1 also received oregovomab as monotherapy 12 weeks after the fifth cycle.

Reporting group title	Control Group
-----------------------	---------------

Reporting group description:

Arm 2: First-line chemotherapy (carboplatin and paclitaxel) in patients with advanced epithelial ovarian, adnexal, or peritoneal carcinoma.

Treatment Arm 2 (40 patients planned) received, sequentially, carboplatin AUC 6 administered IV every 3 weeks (21 days) for 6 cycles, followed by paclitaxel 175 mg/m² IV over 3 hours every 3 weeks for 6 cycles.

Serious adverse events	Treatment Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 46 (19.57%)	7 / 48 (14.58%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Reproductive system and breast disorders			
Pelvic fluid collection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pleural effusion			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Syncope			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Blood and lymphatic system disorders			
Abdominal lymphadenopathy			

subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Anaemia			
subjects affected / exposed	1 / 46 (2.17%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Febrile neutropenia			
subjects affected / exposed	1 / 46 (2.17%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pancytopenia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Intestinal infarction			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Localised intraabdominal fluid collection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Vomiting			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Hepatobiliary disorders			

Cholecystocholangitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 2	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Infections and infestations			
Hepatitis B			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Neutropenic sepsis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Hypomagnesaemia			

subjects affected / exposed	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2

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

Non-serious adverse events	Treatment Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 46 (78.26%)	39 / 48 (81.25%)	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	2 / 46 (4.35%)	3 / 48 (6.25%)	
occurrences (all)	2	3	
Paraesthesia			
subjects affected / exposed	7 / 46 (15.22%)	9 / 48 (18.75%)	
occurrences (all)	7	9	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 46 (8.70%)	3 / 48 (6.25%)	
occurrences (all)	4	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 46 (39.13%)	15 / 48 (31.25%)	
occurrences (all)	18	15	
Leukopenia			
subjects affected / exposed	17 / 46 (36.96%)	17 / 48 (35.42%)	
occurrences (all)	17	17	
Neutropenia			
subjects affected / exposed	21 / 46 (45.65%)	25 / 48 (52.08%)	
occurrences (all)	21	25	
Thrombocytopenia			
subjects affected / exposed	3 / 46 (6.52%)	5 / 48 (10.42%)	
occurrences (all)	3	5	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 46 (15.22%)	6 / 48 (12.50%)	
occurrences (all)	7	6	

Fatigue subjects affected / exposed occurrences (all)	6 / 46 (13.04%) 6	7 / 48 (14.58%) 7	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	8 / 46 (17.39%) 8	5 / 48 (10.42%) 5	
Nausea subjects affected / exposed occurrences (all)	9 / 46 (19.57%) 9	7 / 48 (14.58%) 7	
Vomiting subjects affected / exposed occurrences (all)	3 / 46 (6.52%) 3	2 / 48 (4.17%) 2	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	8 / 46 (17.39%) 8	6 / 48 (12.50%) 6	
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 46 (0.00%) 0	3 / 48 (6.25%) 3	
Myalgia subjects affected / exposed occurrences (all)	2 / 46 (4.35%) 2	3 / 48 (6.25%) 3	
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	3 / 46 (6.52%) 3	0 / 48 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 February 2012	Updated Protocol
21 July 2012	Updated Protocol
07 September 2012	Updated Protocol
08 February 2013	Updated Protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31916979>