Clinical trial results:
NSGO-OV-UMB1; ENGOT-OV30: A phase II umbrella trial in patients with relapsed ovarian cancer.

Summary

EudraCT number	2017-002805-36
Trial protocol	DK FI NO
Global end of trial date	30 November 2021

Results information

Result version number	v1 (current)
This version publication date	10 September 2023
First version publication date	10 September 2023

Trial information

Trial identification

Sponsor protocol code	ENGOT-OV30/NSGO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03267589
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU)
Sponsor organisation address	Blegdamsvej 9 , Copenhagen , Denmark, 2100
Public contact	Medical Director, Mansoor Raza Mirza, Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU), +45 35453311, mansoor.raza.mirza@regionh.dk
Scientific contact	Medical Director, Mansoor Raza Mirza, Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU), +45 35453311, mansoor.raza.mirza@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2021
Global end of trial reached?	Yes
Global end of trial date	30 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective is to obtain preliminary evidence of efficacy of novel agents for the management of relapsed ovarian cancer.

Protection of trial subjects:

The IDSMC was established to provide independent review and assessment of the efficacy and safety data in a systematic manner and to safeguard the interest and safety of the participating patients in the study. The composition of the IDMC consisted of 3 independent individuals, and made recommendations to the Sponsor based on their review to continue or stop the trial based on their assessment of safety information. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the ICH-GCP guidelines. The local principal investigators were responsible for ensuring that the study was conducted in accordance with the protocol, the ethical principles of the Declaration of Helsinki, current ICH guidelines on Good Clinical practice (GCP) and applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Finland: 5
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	12
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Candidates were identified by a member of the treatment team. The investigator screened patients' medical records for suitable candidates. Patients had to sign a specific CD73 ICF. Enrolment occurred only after the patient had signed the ICF and screening assessments and eligibility criteria were completed. Recruitment from Q2 2018 - Q2 2019.

Pre-assignment

Screening details:

Subjects underwent CD73 expression evaluation to ensure positive tumor cell CD73 expression. During pre-screening, patients were required to sign the ICF, fulfil the eligibility criteria and consent to give an archival tumor sample for CD73 screening. Re-screening at a later date at investigator's discretion was possible, though not more than once.

Period 1

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

Arms

Arm title	Cohort A

Arm description:

25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab.

Arm type	Experimental
Investigational medicinal product name	MEDI9447
Investigational medicinal product code	
Other name	Oleclumab
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received MEDI9447 3000 mg every 2 weeks via IV infusion. Subjects will remain on therapy until unacceptable toxicity, documentation of disease progression, subject withdrawal, or completion of the study.

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received durvalumab 1500 mg every 4 weeks via IV infusion. A dose of 1500 mg (for patients >30kg in weight) was administered using an IV bag containing 0.9% (w/v) saline or 5% (w/v) dextrose, with a final durvalumab concentration ranging from 1 to 20 mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter. Subjects will remain on therapy until unacceptable toxicity, documentation of disease progression, subject withdrawal, or completion of the study.

Number of subjects in period 1	Cohort A
Started	25
Completed	2
Not completed	23
Death	19
Other	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall period
Reporting group description:	
25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab.	

Reporting group values	Overall period	Total	
Number of subjects	25	25	
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)	12	12	
From 65-84 years	13	13	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	64.7		
standard deviation	± 8.8	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	0	0	
Race Units: Subjects			
White	23	23	
Asian	2	2	
Previous cancer Units: Subjects			
No	25	25	
Yes	0	0	
Any comorbidity Units: Subjects			
No	24	24	
Yes	1	1	
Number of relapses Units: Subjects			
1st relapse	5	5	
≥2 relapses	20	20	
FIGO Units: Subjects			

Stage IV A	6	6	
Stage IV B	5	5	
Unknown	1	1	
Stage I	3	3	
Stage III	10	10	
Prior chemotherapy Units: Subjects			
No	0	0	
Yes	25	25	
Prior chemo type Units: Subjects			
Adjuvant	4	4	
1st line	11	11	
2nd line	3	3	
3rd line	1	1	
Not reported	6	6	
BRCA mutation Units: Subjects			
No	19	19	
Yes	3	3	
Missing	3	3	
ECOG Performance Status Units: Subjects			
ECOG Performance Status 0	10	10	
ECOG Performance Status 1	15	15	

End points

End points reporting groups

Reporting group title	Cohort A

Reporting group description:

25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab.

Primary: Disease control rate (DCR) (CR+PR+SD)

End point title	Disease control rate (DCR) (CR+PR+SD)[1]

End point description:

The analysis of DCR will be performed by calculating the point estimate of the percentage of patients which achieve complete or partial response or stable disease for at least 16 weeks, assessed according to RECIST 1.1 criteria.

End point type	Primary

End point timeframe:

Disease Control Rate (DCR = Complete Response (CR), Partial Response (PR) or Stable Disease (SD) at 16 weeks).

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: Only endpoint data from one arm (arm A) is reported. According to the EudraCT manual, it is therefor not mandatory to report the statistical analysis related to an endpoint (only one arm).

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent				
number (confidence interval 95%)	0.32 (0.14 to 0.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-Free Survival (PFS)

End point title	Median Progression-Free Survival (PFS)

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.
Median PFS estimated by Kaplan-Meier method using RECIST v. 1.1

End point type	Secondary

End point timeframe:

Median Progression-Free Survival (PFS) by RECIST v1.1 until end of observation.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: month				
median (standard error)	2.73 (± 0.533)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Patients who were alive at the time of the analysis were censored at the date of their last follow-up assessment. Patients without follow-up assessment were censored at the day of their last dose and patients with no post baseline information were censored at the time of their first administration of treatment drugs. OS was be estimated and tested along the same lines as PFS.
Overall survival estimated by Kaplan-Meier methods

End point type	Secondary

End point timeframe:

OS is defined as the time from the date of inclusion/randomization to the date of death, regardless of the cause of death, or until end of observation.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: month				
median (standard error)	9.59 (± 2.198)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) according to RECIST v1.1

End point title	Objective Response Rate (ORR) according to RECIST v1.1

End point description:

Objective response rate defined as the proportion of subjects achieving a best overall objective response according to RECIST v1.1 of PR or CR.
The analysis of the response rate is performed by calculating the point estimate of the percentage of patients which achieved complete or partial response assessed according to RECIST 1.1.

End point type	Secondary

End point timeframe:

Objective Response Rate (ORR) according to RECIST v1.1 at 16 weeks.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent				
number (confidence interval 95%)	0.045 (0.001 to 0.228)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

NB: Duration of Response (DoR) endpoint is not reported, as there is only one responder.

End point type	Secondary

End point timeframe:

DoR is the time between the initial response to therapy and subsequent disease progression or relapse. DoR can be estimated and tested along the same lines as PFS.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	22[2]			
Units: month				
median (standard error)	0 (± 0)			

Notes:

[2] - DoR is not reported, as there was only one responder

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 6 months by RECIST v. 1.1

End point title	Progression-free survival (PFS) at 6 months by RECIST v. 1.1

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.

6-month PFS by RECIST v. 1.1 estimated by Kaplan-Meier method

End point type	Secondary

End point timeframe:

Progression-Free Survival (PFS) by RECIST v1.1 at 6 months

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent				
number (confidence interval 95%)	0.20 (0.07 to 0.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 12 months by RECIST v. 1.1

End point title	Progression-free survival (PFS) at 12 months by RECIST v. 1.1

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.
12-month PFS by Immune-RECIST estimated by Kaplan-Meier method

End point type	Secondary

End point timeframe:

Progression-Free Survival (PFS) by RECIST v1.1 12 months

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: N/A				
number (confidence interval 95%)	0.04 (0.003 to 0.170)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-free survival (PFS) by Immune-RECIST

End point title	Median Progression-free survival (PFS) by Immune-RECIST

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.
Median PFS estimated by Kaplan-Meier method using Immune-RECIST.

End point type	Secondary

End point timeframe:

Median PFS by Immune-RECIST until end of observation.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: month				
median (standard error)	3.29 (± 0.625)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 6 months by Immune-RECIST

End point title	Progression-free survival (PFS) at 6 months by Immune-RECIST

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.

End point type	Secondary

End point timeframe:

PFS by Immune-RECIST at 6 months.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: month				
number (confidence interval 95%)	0.24 (0.10 to 0.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 12 months by Immune-RECIST

End point title	Progression-free survival (PFS) at 12 months by Immune-RECIST

End point description:

End point type	Secondary

End point timeframe:

PFS by Immune-RECIST at 12 months.

End point values	Cohort A			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: month				
number (confidence interval 95%)	0.04 (0.003 to 0.170)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events must be reported to sponsor from day 1 of the treatment and until 28 days after the last date of treatment.

Adverse event reporting additional description:

The investigator is responsible for ensuring that all adverse events observed by the investigator or report-ed by subjects are properly recorded in the subjects' medical records and the electronic case report form.

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	Cohort A

Reporting group description:

25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab

Serious adverse events	Cohort A		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 25 (60.00%)		
number of deaths (all causes)	19		
number of deaths resulting from adverse events	1		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 19		
Pain			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 19		
Other			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences causally related to treatment / all	3 / 10		
deaths causally related to treatment / all	0 / 19		
Blood and lymphatic system disorders			

Neutropenia				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 19			
Gastrointestinal disorders				
Ascites				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 19			
Constipation				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 19			
Gastrointestinal perforation				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 19			
Ileus				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 19			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 19			
Pleural effusion				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 19			

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

Non-serious adverse events	Cohort A		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 25 (96.00%)		
Investigations			
Blood creatine increased			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Peripheral motor neuropathy			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	17		
Fever			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	6		
Pain			
subjects affected / exposed	14 / 25 (56.00%)		
occurrences (all)	20		
Decreased appetite			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	9		
Edema			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
Other			
subjects affected / exposed	23 / 25 (92.00%)		
occurrences (all)	76		

Gastrointestinal disorders			
Ascites			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	7		
Constipation			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	5		
Ileus			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	8 / 25 (32.00%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
Pleural effusion			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	10		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	6		
Urinary tract infection			

subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	 3 / 25 (12.00%) 4		
Metabolism and nutrition disorders Hypomagnesaemia subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all)	 2 / 25 (8.00%) 3 4 / 25 (16.00%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported