MOONSTONE/GOG-3032: A Phase 2, Open-Label, Single-Arm Study to Evaluate the Efficacy and Safety of Niraparib + Dostarlimab in Patients with Platinum-Resistant Ovarian Cancer

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Background

Therapeutic area

Ovarian cancer has one of the highest mortality rates of all gynaecologic cancers[1]

While initial response to surgery and first-line platinum-based chemotherapy might be favourable, up to 70% of patients relapse and the majority of tumours become platinum resistant[2,3]

The anti-VEGF monoclonal antibody, bevacizumab, is approved for treatment of recurrent platinum-resistant ovarian cancer in combination with single-agent chemotherapy[3]

However, there is still a strong clinical need for new treatment options[2]

Niraparib

Niraparib is a PARPi approved for:

- First-line maintenance treatment of adult patients with platinum-sensitive advanced epithelial ovarian, fallopian tube or primary peritoneal cancer (USA)[4]
- Maintenance treatment of adult patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer (USA and EU)[4,5]
- Treatment of adult patients with advanced ovarian, fallopian tube or primary peritoneal cancer who have received ≥3 prior chemotherapy regimens whose cancer is associated with HRD-positive status defined by a deleterious or suspected deleterious *BRCA* mutation or genomic instability and progression >6 months after response to last platinum-based chemotherapy (USA)[4]

Niraparib monotherapy has shown antitumour activity in patients with platinum-refractory ovarian cancer, in a Phase II study of late-line treatment.[4,6] This included efficacy in patients with *BRCA* wild-type tumours who, in advanced ovarian cancer, have worse survival outcomes than those with *BRCA* mutations[6,7]

Niraparib in combination regimens

Dostarlimab is an anti–PD-1 humanised monoclonal antibody that binds with high affinity to the PD-1 receptor, effectively blocks interaction with the PD-1 ligands (PD-L1 and PD-L2), and has shown activity in solid tumours, including in patients who have progressed after a platinum-based regimen[8,9]

PARPi + anti–PD-1 combinations have shown synergistic antitumour effect, regardless of *BRCA* mutation status[10,11]

Trial objective

The objective of this study is to evaluate the safety and efficacy of niraparib + dostarlimab in patients with advanced, relapsed, high-grade, *BRCA* wild-type platinum-resistant ovarian cancer who have progressed and have received prior bevacizumab

Study population

Key inclusion criteria

- Female, ≥18 years of age
- Recurrent high-grade serous, endometrioid or clear cell ovarian, fallopian tube or primary peritoneal cancer
- Have received 1−3 lines of prior therapy with platinum, taxane and bevacizumab
- Have had disease progression <6 months from the last administered platinum therapy (as evidenced by radiographic progression per RECIST v.1.1[12])
- Measurable disease (according to RECIST version v.1.1[12])
- ECOG performance status of 0 or 1
- Adequate organ function

Key exclusion criteria

- Prior treatment with a PARPi or anti–PD-(L)1 or anti–PD-L2 agent
- Known or suspected deleterious germline *BRCA* mutations, including *BRCA* mutations within the tumour
- Disease progression within 3 months (as evidenced by radiographic progression per RECIST v.1.1[12]) of first-line platinum therapy

Methods

The MOONSTONE study (NCT03955471) is:

2 Phase II

Open-label

Single-arm

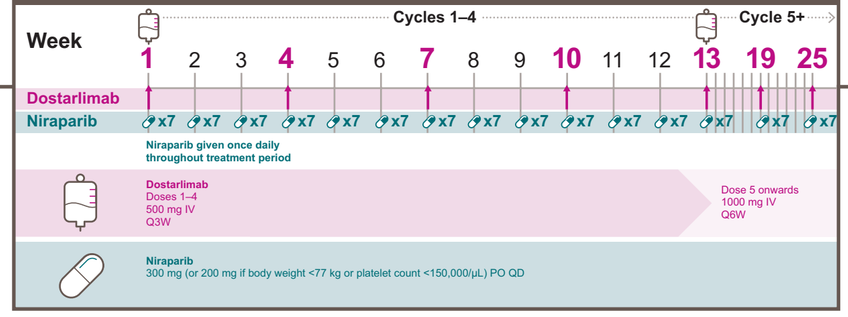
Multicentre in USA

Patients
Approximately 150 with platinum-resistant ovarian cancer, including ~75 with PD-L1-positive tumours

Screening
Day −28 to −1

Treatment period

Day 1 to disease progression or unacceptable toxicity (up to 3 years)*



Safety follow-up
30 ± 7 days after last dose of study treatment

Survival assessment
90 ± 14 days after last dose of study treatment

*Other reasons for discontinuation include withdrawal of consent, investigator's decision or death. Patients who discontinue one of the treatments due to adverse events will be able to continue treatment with the second agent until disease progression or unacceptable toxicity.

Study objectives and endpoints

*Primary endpoint**

- ORR assessed by investigator
  - In the overall population
  - In the subset of patients with PD-L1+ tumours

*Key secondary endpoints**

- DoR
- PFS
- OS
- DCR
- ORR assessed by an independent review committee
- Safety and tolerability of combination treatment

Exploratory endpoints

- Efficacy in patients with confirmed *BRCA* wild-type tumours*†
- Duration of disease control in patients with best overall response of SD, PR or CR
- HRQoL as measured by FOSI
- Disease-related and treatment-related biomarkers of response, including:
  - Measures of homologous recombination repair pathway defects
  - Optimal PD-L1 levels for efficacy

*Response evaluated using RECIST v1.1[12] in the overall population and in the subset of patients with PD-L1+ tumours; †definitive germline *BRCA* mutation status per tumour sample obtained during study.

Current status

- **Currently recruiting**
- **Primary completion: September 2021**
- **Study completion: February 2024**

Abbreviations

BRCA, breast cancer gene; CR, complete response; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; FOSI, Functional Assessment of Cancer Therapy: Ovarian Symptom Index; HRD, homologous recombination deficiency; HRQoL, health-related quality of life; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PD-1, programmed cell death receptor 1; PD-L, programmed cell death ligand; PFS, progression-free survival; PR, partial response; PO, oral; Q3W, every 3 weeks; Q6W, every 6 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; VEGF, vascular endothelial growth factor

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