MONO-OLA1: a randomized, Phase III study of olaparib maintenance monotherapy in patients with BRCA wild-type advanced ovarian cancer following response to first-line platinum-based chemotherapy

Introduction

• The aim of MONO-OLA1, a randomized Phase III study, is to assess the efficacy and safety of olaparib maintenance monotherapy, compared with placebo, in patients with newly diagnosed BRCA1 and BRCA2 wild-type (BRCAwt) advanced ovarian cancer following clinical complete or partial response to first-line platinum-based chemotherapy.

• Results from the SOL01 study (NCT01844986) demonstrated significant progression-free survival (PFS) benefits to patients with newly diagnosed BRCA-mutated (BRCAm) ovarian cancer treated with maintenance olaparib. As a result of this study, maintenance olaparib was approved in patients with newly diagnosed advanced ovarian cancer in clinical complete or partial response to first-line platinum-based chemotherapy and is now the standard of care in this population.1

• Approximately 60–80% of patients with high-grade serous ovarian cancer are BRCAwt.2,3 The majority of these patients experience a high unmet medical need due to limited treatment options.

• Maintenance therapy with a PARP inhibitor, with or without bevacizumab, has been shown to provide benefit to patients with newly diagnosed advanced ovarian cancer without a BRCAm.3,4

• The aim of this MONO-OLA1 study (NCT04884360) is to assess the efficacy and safety of maintenance olaparib, compared with placebo, in patients with newly diagnosed BRCA1 and BRCA2 wild-type ovarian cancer with clinical complete or partial response to first-line platinum-based chemotherapy.

Key inclusion criteria

• Aged ≥ 18 years.

• Histologically confirmed newly diagnosed high-grade serous or endometrioid ovarian cancer, fallopian tube cancer, or primary peritoneal cancer (FIGO International Federation of Gynecology and Obstetrics [FIGO] stage III–IV).

• Patients must fulfill any of the following surgical criteria:
  - Stage III: primary debulking surgery with macroscopic residual disease following surgery, neoadjuvant chemotherapy, or inoperable.
  - Stage IV: primary debulking surgery regardless of residual disease, neoadjuvant chemotherapy, or inoperable.

• Confirmed BRCAwt status as per centrally performed tumor BRCA testing.

• Clinical complete or partial response as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 following first-line platinum-based chemotherapy.

• Patients should not have received bevacizumab with first-line chemotherapy or be due to receive bevacizumab maintenance therapy.

• Minimum life expectancy of 16 weeks.

Key exclusion criteria

• Prior exposure to PARP inhibitors, including olaparib.

• Complete cytoreduction following primary debulking surgery in patients with stage III disease.

Methods

MONO-OLA1 is a Phase II randomized, double-blind, placebo-controlled, international study (Figure 1).

• Planned sample size: 420 women.

• Patients will be randomly assigned (2:1) to receive maintenance olaparib (300 mg twice daily [bid]) or placebo tablets.

• Planned duration of follow-up is 2 years or until disease progression.

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Primary endpoints

• Investigator-assessed PFS by RECIST v1.1 in BRCAwt HRD-positive patients.

Secondary endpoints

• Assessment of the following in BRCAwt HRD-positive and BRCAwt patients:
  - Overall survival (OS)
  - Second PFS
  - Time to second subsequent therapy or death
  - Time to discontinuation of study intervention or death
  - Time to earliest progression by RECIST v1.1 or cancer antigen 125 or death

Key exploratory endpoints

• Translational analyses to identify predictive biomarkers of response and resistance to olaparib.

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References