

# PAOLA1

## Platine, Avastin and Olaparib in first line advanced high grade ovarian carcinoma patients

Randomized, Double-blind, Phase III Trial of olaparib vs. Placebo in combination with bevacizumab in women who have not progressed after first-line chemotherapy plus bevacizumab for advanced high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer

# RATIONALE

- ▶ Bevacizumab in first line treatment in combination with chemotherapy and in maintenance: GOG 218 and ICON7 trials
- ▶ Olaparib in maintenance after platinum-based chemotherapy in high grade serous platinum-sensitive relapsed ovarian cancer: D0810C00019 study (HR: 0.35)
- ▶ **the premise of combining olaparib and bevacizumab is based on the rationale that direct targeting of PARP by olaparib and indirect sensitization to olaparib by acquisition of HR defects by bevacizumab will be therapeutically beneficial**

## ➤ PRIMARY OBJECTIVE

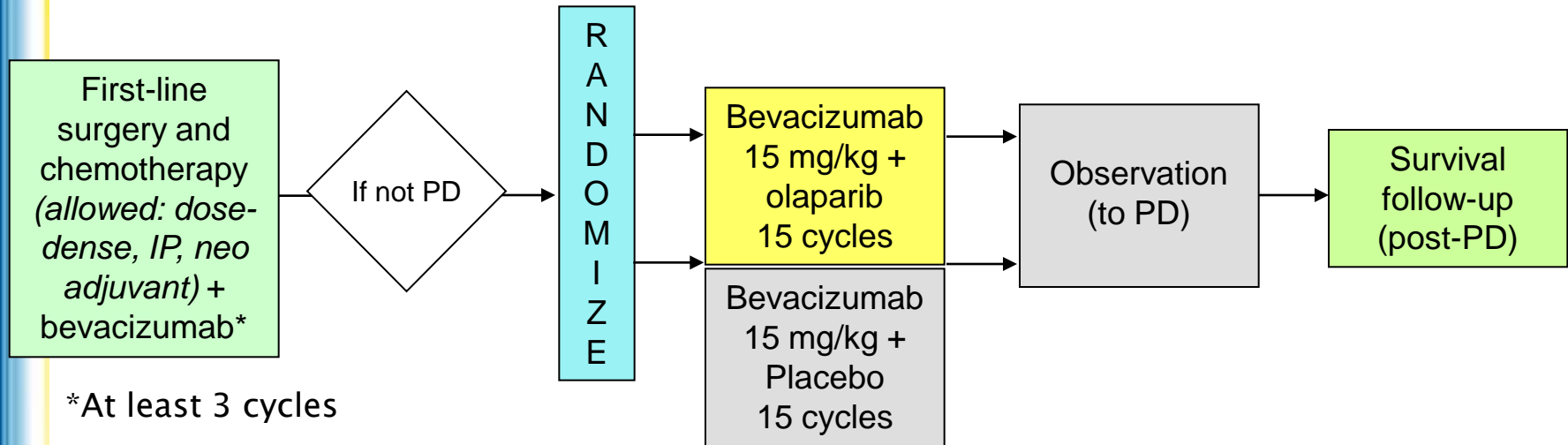
To determine the efficacy by progression free survival (PFS) according to modified Response Evaluation Criteria in Solid Tumours (RECIST 1.1)

## ➤ SECONDARY OBJECTIVE

- ✓ Overall survival (OS).
- ✓ Post progression survival (PFS n°2)
- ✓ Rate of deterioration of Health-related Quality of Life (HRQoL) as assessed by the trial outcome index (TOI) of the Functional Assessment of Cancer Therapy – Ovarian (FACT-O) in advanced HGS ovarian cancer patients
- ✓ Safety and tolerability
- ✓ Biological markers

# Study Design

- ▶ Phase III randomized, placebo-controlled, double-blind, multicenter
- ▶ Olaparib tablets administered at 300 mg daily for up to 15 cycles.



Estimated median months from diagnosis to randomization (7 months)

## Stratification factors:

Groups / regions, response to CT plus bev (CR/PR vs. SD) including the potential effect of interval debulking versus front line debulking effect, BRCA germ line mutation (yes/no/unknown)

# Inclusion / Exclusion Criteria

## Main inclusion criteria

- ▶ Female aged  $\geq 18$  years at the time of study inclusion
- ▶ Patients with newly diagnosed, histologically confirmed, FIGO stage IIIB–IV high grade (based on local histopathological findings) epithelial ovarian cancer, primary peritoneal cancer and / or fallopian–tube cancer.
- ▶ Stage III patients should have had one attempt at optimal debulking surgery (upfront or interval debulking). Stage IV patients must have had either a biopsy and/or upfront or interval debulking surgery.
- ▶ Patients must have completed a minimum of 6 and a maximum of 9 cycles of first line platinum–based therapy and at least 3 cycles with bevacizumab. before randomization to the study;
- ▶ Before randomisation patients must be in CR, PR or SD with chemotherapy plus bevacizumab regimen



# Statistical Consideration/Endpoints

## ▶ Primary Endpoint:

- ▶ **Sample size determination:** Improvement in median PFS\* from 15 months (arm Bev alone) to 21 months (arm arm Bev + Ola) (HR=0.71)
- ▶ with a recruitment duration of 2 years and follow up 2 years (total duration of study 4 years),
- ▶ 251 patients/arm are needed (for a total of 371 events), with a bilateral alpha of 5% and 90% power.
- ▶ N = 502
  
- ▶ \*estimated PFS of patients under bevacizumab maintenance (but who did not progressed under chemotherapy) from GOG218 & ICON7 trial