#1539

PHASE II STUDY TO ASSESS THE EFFICACY OF NIRAPARIB RECHALLENGE AFTER COMPLETE SECONDARY CYTOREDUCTION IN OVARIAN CANCER PATIENTS WITH OLIGOMETASTATIC PROGRESSION: THE ANALLISA STUDY

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José Muñoz-Langa[1], María Quindos[2], Fernando Gálvez Montosa[3], Jorge Bartolomé[4], María Masvidal Hernández[5], Mª Mar Gordón Santiago[6], Carmen García-Durán[7], Marta Beltran[8], Felipe Slebe[8], Simona Iacobucci[8], Jose Antonio Guerrero[8], Olga Boix[8], Eva Guerra[9], Ainhoa Madariaga[10], Andrés Redondo[11], Alfonso Cortés-Salgado[9]

[1]Hospital Arnau de Vilanova de Valencia, Valencia, Spain; [2]Medical Oncology Department, Complexo Hospitalario Universitario de A Coruña. Biomedical Research Institute (INIBIC), A Coruña, Spain; [3]Hospital Universitario de Jaén, Jaén, Spain; [4]Hospital Clínico San Carlos, Madrid, Spain; [0]Hospital Universitari Sant Joan de Reus, Tarragona, Spain; [6]Hospital Universitario Virgen Macarena, Sevilla, Spain; [7]Gynecological Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Val d'Hebron, Barcelona, Spain; [8]Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil); [9]Hospital Universitario Ramón y Cajal, Madrid, Spain; [10]Hospital Universitario 12 de Octubre, Madrid, Spain; [11]Hospital Universitario La Paz, Madrid, Spain

BACKGROUND

- Maintenance with PARP inhibitors (PARPi) is the standard of care for high-grade ovarian cancer (OC) patients who are in response to frontline platinum-based therapy, particularly for those with *BRCA* mutations or homologous recombination deficiency (HRD) **[1-3].**
- However, most patients progress during or after PARPi, with over 90% experiencing oligometastatic progression (OMP) **[4]**, defined as ≤5 lesions per ASCO/ESTRO consensus.
- The optimal treatment strategy for OC patients with OMP remains unclear, representing an unmet medical need.
- Previous retrospective studies have shown the benefit of combining local treatment for oligoprogressive lesions and continuation of systemic therapy with iPARP **[5-6]**.
- The ANALLISA study is prospectively evaluating the efficacy and safety of a niraparib rechallenge in patients with OC and OMP after complete secondary cytoreduction, progressing during or after the first maintenance PARPi.

TRIAL DESIGN

- This is a multicenter, single-arm, proof-of-concept, phase II trial.
- Patients will receive niraparib treatment after a complete secondary cytoreduction until progressive disease, treatment discontinuation, or death.

STATISTICS

- Sample size was based on an exponential maximum likelihood estimation test with one-sided alternative hypothesis of median PFS ≥9 months and null hypothesis of median PFS ≤5 months, requiring 18 events to achieve 80% power at a 5% Type I error.

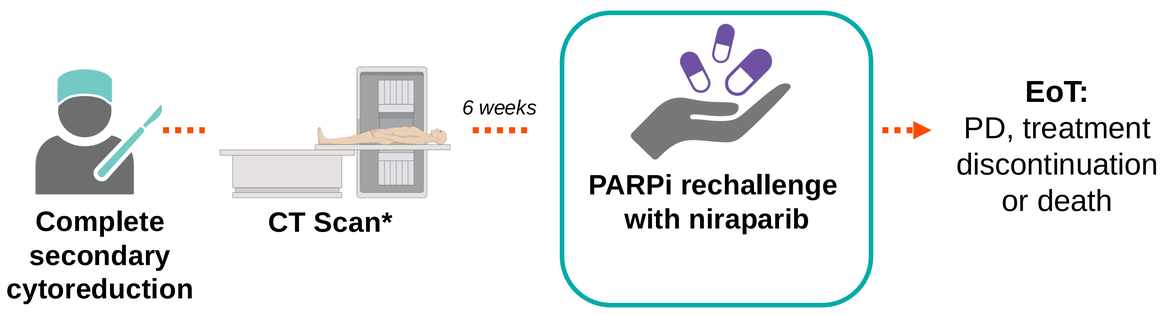
TRIAL ENROLLMENT

- The ANALLISA study was opened to accrual in July 2024 and is currently recruiting in 9 institutions from Spain.

STUDY DESIGN

KEY INCLUSION CRITERIA

- Age ≥18 years old
- Histologically confirmed high grade OC who experience an OMP during or after the first maintenance therapy with any PARPi.
- OMP defined as up to 5 lesions.
- Patients must have undergone secondary cytoreductive surgery with centrally confirmed no evidence of macroscopic residual tumor after surgery (complete resection).
- Patients must have either normal or up to 2 x ULN CA-125 level
- Known *BRCA1/2* and HRD status.
- Prior PARPi monotherapy or PARPi + bevacizumab as maintenance treatment§
- ECOG performance status of 0-1.
- Adequate hematologic and organ function.



** One CT scan of thorax, abdomen, pelvis and clinically indicated areas will be evaluated by central review.*

Treatment

- 300 or 200 mg PO, QD, based on weight or platelet count in 28-day cycles
- If patient has received niraparib as previous PARPi, the starting dose would depend on the previous dose.

Samples

- at primary and secondary surgeries
- at baseline, every 3 cycles and at the EoT

PRIMARY ENDPOINT

- PFS as per RECIST v.1.1.

SECONDARY ENDPOINTS

- PFS according to biomarker status (*BRCA*m, *BRCA*wt, HRD and HRP), PFS by CA-125, PFS2, TFST, OS, safety and toxicity as per NCI-CTCAE v.5.0.

EXPLORATORY ENDPOINT

- Correlation analysis: PFS vs. prior PARPi maintenance; PFS vs. previous benefit to PARPi; changes in ctDNA levels vs. outcomes; PARPi-related biomarkers vs. outcomes

§*Patients must have benefited from prior PARPi, defined as at least 12 months of exposure (18 months for those with a BRCA1/2 mutation) from PARPi maintenance initiation to the date of OMP.*

***BRCA*:** breast cancer gene; **CA-125:** cancer antigen 125**; CT:** computed tomography; **ECOG:** Eastern Cooperative Oncology Group; **EoT:** end of treatment; **HRD:** homologous recombination deficiency; **HRP:** homologous recombination proficiency; **NCI-CTCAE:** National Cancer Institute-Common Terminology Criteria for Adverse Events; **OC:** ovarian cancer; **OMP:** oligometastatic progression; **OS:** overall survival; **PARPi:** poly (adenosine diphosphate [ADP] ribose polymerase inhibitor); **PD:** progressive disease; **PO:** orally; **PFS:** progression-free survival; **QD:** once daily; **RECIST:** Response Evaluation Criteria in Solid Tumors; **TFST:** time to first subsequent therapy; **ULN:** upper limit of normal

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CONTACT INFORMATION

Dr. Alfonso Cortés alfonso.cortes@external.medsir.org

MEDSIR MEDICA SCIENTIA INNOVATION RESEARCH ONCOCLÍNICAS