TEDOVA/GINECO-OV244b/ENGOT-ov58 trial: Neo-epitope based vaccine OSE2101 alone or in combination with Pembrolizumab vs best supportive care (BSC) as maintenance in platinum-sensitive recurrent ovarian cancer with disease control after platinum.

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INTRODUCTION / BACKGROUND

- Besides PARP inhibitors and bevacizumab, there are **no approved maintenance therapies after platinum based chemotherapy** for patients with a **platinum sensitive relapsed epithelial ovarian cancer (OC)**.
- Immune checkpoint inhibitors (ICI) as single agents have limited activity in OC.
- One attractive strategy is to **turn OC from immunogenic "cold" to "hot" tumors** via vaccination with tumor-associated antigens (TAAs).
- **OSE2101** is a **multiple-neoepitope vaccine** restricted to HLA-A*02-positive patients (45% of OC patients) targeting 5 TAAs: TP53, MAGE2, MAGE3, CEA and HER2. These neo-epitopes are modified to increase both major histocompatibility complex and the T cell receptor binding affinity.
- The proof of concept for this approach was recently demonstrated with OSE2101 improving overall survival in a phase III trial in lung cancer progressing after ICI (Besse *et al.* 2021[1]). **The combination of OSE2101 with an ICI may most effectively harness anti-tumor immunity.**

METHODOLOGY

- TEDOVA is an international randomized open-label, **phase II trial** evaluating **the benefit of maintenance** by OSE2101 alone or in combination with PD1 inhibition (pembrolizumab) after **platinum based chemotherapy in relapsed OC**, **previously treated** with **bevacizumab** (if eligible) and a **PARP inhibitor** (if eligible).
- Patients with clinical or radiological relapse of a platinum sensitive OC **regardless of the number of prior lines of platinum-based chemotherapy**, **as long as each prior line fulfilled the platinum sensitive criteria** defined as complete response, partial response or stable disease according RECIST 1.1 at the end of a platinum-based chemotherapy. Patient must have received **at least 4 cycles of platinum**.
- Patients with CR/PR/SD at the end of chemotherapy are randomized (1:1:2) to: **Observation/BSC (Arm A)**, **OSE2101 alone (Arm B)**, or **OSE2101 in combination with pembrolizumab (Arm C).**
- Experimental treatments are continued until progression, or intolerance, for up to 2 years.
- 180 HLA-A*02 positive patients will be randomized. HLA-A*02 negative patients will be followed in a separate observational cohort.

MAIN ENDPOINTS

- The **primary endpoint** is **progression-free survival (PFS)** assessed by the investigator (RECIST1.1)
- Secondary endpoints include overall response rate, safety, time to subsequent first or second treatment (TTST-1, TTST-2) and overall survival.
- Exploratory objective include predictive biomarkers or clinical outcomes for the Observational cohort

STATISTICS

- The sample size is calculated to provide 90% power to detect an improvement in PFS for Arm C vs Arm A with a HR of 0.57.
- Three one-sided Log-rank tests will be considered in a pre-defined sequence:
  - H1: C (OSE2101+pembrolizumab) vs A (BSC)
  - H2: C (OSE2101+pembrolizumab) vs B (OSE2101)
  - H3: B vs A.

  The type I error will be α=5%. The type II error will be β=10%. Tests will be one-sided
- A total of **121 events** (progression or deaths) **is requested to carry out the first test of H1**. Assuming that the accrual will be completed in 2 years and each patient is followed up for a minimal duration of 1 year **180 patients have to be randomized** between arm A (nA=45), B (nB=45) and C (nC=90) to observe those events.

ACCRUAL AND STUDY CALENDAR

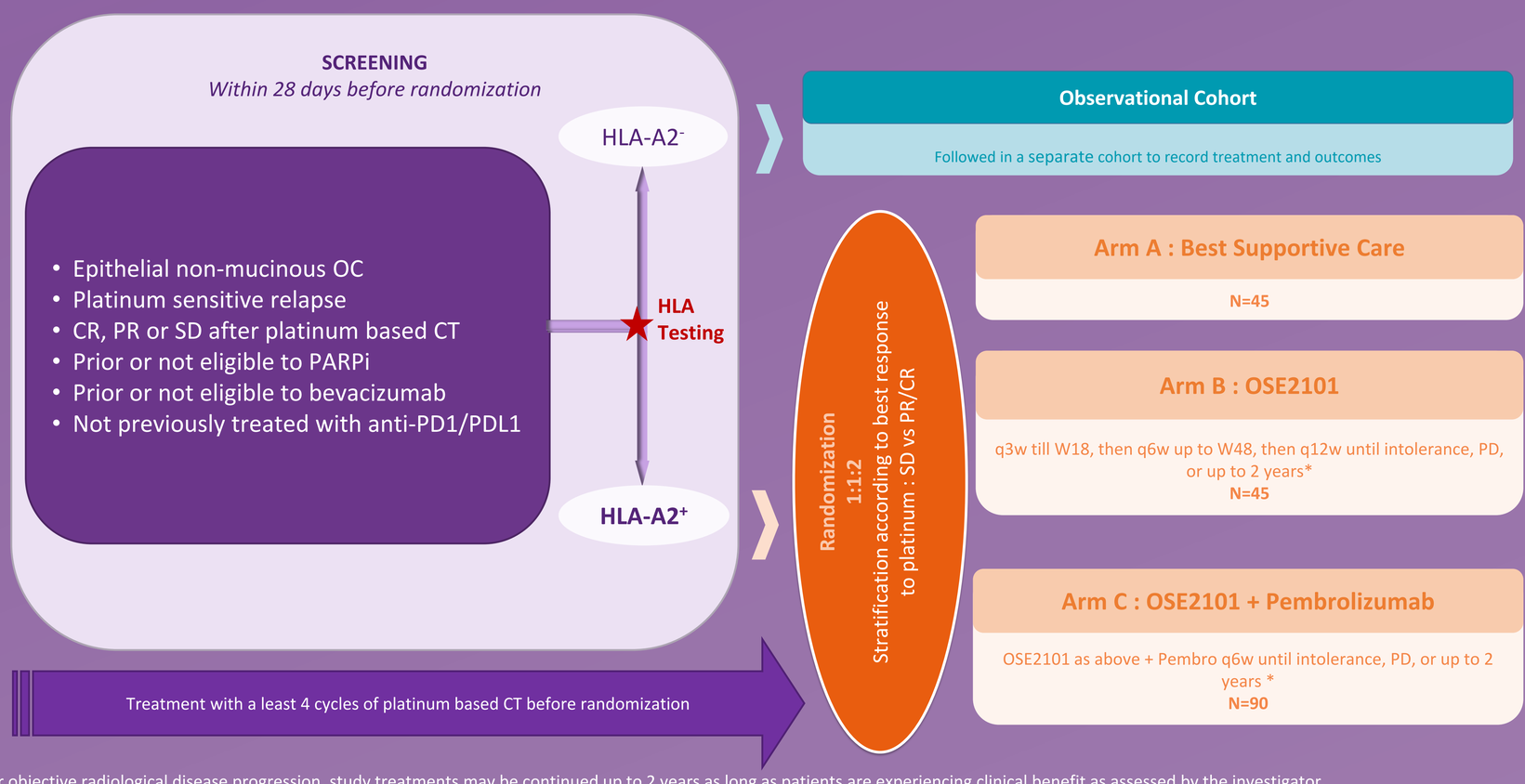
- Study is recruiting in France, submissions to regulatory authorities ongoing in Belgium and Germany.
- The first patient was randomized in August 2021
- Until 11th May 2022, **50 patients have been registered** including 21 HLA-A*02 positive patients. **15 patients have been randomized** and 6 are screen failed. The 23 HLA-A*02 negative patients except 2 (screen failed) are followed in the observational cohort.
- The inclusion period is planned for a duration of 24 months

Next steps	Timelines
Planned accrual period	**24 months**
Treatment duration	**Max 24 months**
Estimated Last patient last visit (LPLV)	**Q2 2025 (estimated as event-driven trial)**

CONCLUSION

- In this unmet need situation, **TEDOVA study** will explore the **efficacy and safety** of **maintenance by OSE2101 alone or in combination with PD1 inhibition** (pembrolizumab) after platinum based chemotherapy in relapsed OC, **previously treated** with **bevacizumab** (if eligible) and a **PARP inhibitor** (if eligible).
- Recruitment to TEDOVA Study is ongoing with **15 patients randomized on the 180 expected**.

STUDY DESIGN



PARTICIPATING GROUPS

* Even after objective radiological disease progression, study treatments may be continued up to 2 years as long as patients are experiencing clinical benefit as assessed by the investigator.
After 24 months of treatment, and in case the investigator thinks that the patient may get a clinical benefit by prolonging the experimental treatment OSE2101, the investigator and the sponsor will discuss the best option of how to pursue this treatment.

REFERENCES

[1] Besse B, Garcia MR, Cobo MA, Quoix E, Madroszyk A, Felip E, et al. LBA47 - Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final results of phase III Atalante-1 randomised trial. Annals of Oncology 2021;32(suppl_5) : S1283-S1346

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