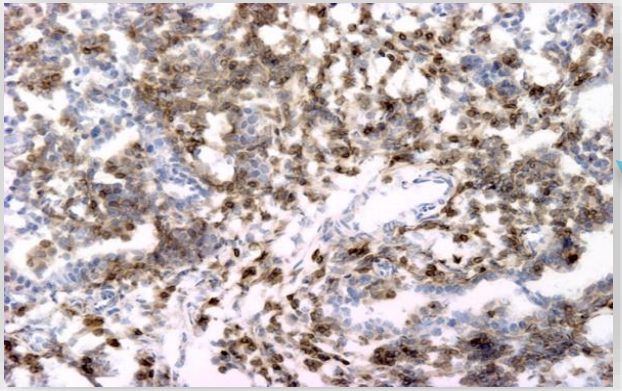
ATALANTE
Atezolizumab and Avastin
in late recurrent disease

ATezolizumab and Avastin in LAte recurreNT diseasE
ENGOT-ov29

A randomized, double-blinded, phase III study of atezolizumab versus placebo in patients with late relapse of epithelial ovarian, fallopian tube, or peritoneal cancer treated by platinum-based chemotherapy and bevacizumab

Sponsor: ARCAGY-GINECO
ENGOT model A
Lead group: GINECO (PR JE Kurtz)
Co-lead group : ISGO (Pr J Korach)

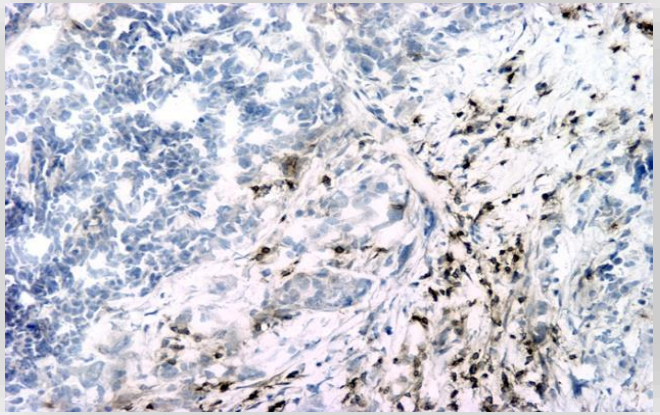
Intraepithelial TILs define two specific subsets of ovarian cancer patients



TIL-rich
55%

T-lymphocytes are present , but **not working**

Anti-PDL1



TIL-poor
45%

T-lymphocytes are just **absent in the tumor**!

Anti-VEGF

ATALANTE

Atezolizumab and Avastin in late recurrent disease

Recurrent late relapse

N=405

- Non-mucinous histology
- TFI p (platinum-free interval)>6 months
- One or 2 prior lines of Cx
- ECOG ≤ I

BIOPSY

Stratification factors

- **PD-L1 expression**
- TFIp (6-12, > 12 mos)
- Chemotherapy cohort

R
I:2

Carboplatin-based chemotherapy

Avastin (BEV) +Placebo

b 12 24 48 72 96

PD

Confirmatory CT-Scan

Avastin (BEV)+ATEZOLIZUMAB

PD

Confirmatory CT-Scan

Interim safety analysis
n=45 après C2

Chemotherapy-based schedule options (investigator's choice): carboplatin AUC5 + paclitaxel (175mg/m² q3wks) or gemcitabine (1000 mg/m² D1&D8 q3wks) or PLD* (30mg/m² q 4wks). BEV 15mg/kg q3 wks or 10mg/kg q2 wks. ATEZO/PLACEBO: 1200mg, I.V q3wks or 800mg q2wks.*

objectives

- **Primary: efficacity of atezolizumab + bev & chemo vs Bev + chemo**

  - RECIST PFS from median of 13 to 18.6 months (HR: 0.70) alpha:0.05, beta:0.8, two-sided

  - and supported by secondary endpoints: TSST and QoL + PROs (EORTC QLQ-30 and OV28).

Secondary objectives

- **Safety**

- ORR/PFS according to RECIST v1.1 and irRECIST (validation)
- Efficacy in PD-L1+ve and PD-L1-ve
- OS
- ressource use (EQ-5D)

STUDY STATUS

- First patient In: Q3 2016
- Last patient In: Q4 2018
- Recruitment period: 30 months
- Last patient last visit: Q2 2021
- Site number: 100
- Number of patients: 405

Submision to French competent authorities: 17/02/2016
ENGOT groups will be contacted by end of March

Question

- In the late relapse setting (> 6 months), what would be the best QoL and PRO endpoints for OC patients treated with immunotherapy ?

Back up slides

INCLUSION CRITERIA

- Histologically confirmed non-mucinous epithelial ovarian cancer, primary peritoneal adenocarcinoma and / or fallopian-tube adenocarcinoma

- Known PD-L1 status on fresh mandatory biopsy sent to central laboratory as a formalin-fixed, paraffin-embedded (FFPE) sample.

- Disease relapsed more than 6 months from the last dose of platinum before randomization

- One or 2 prior lines of chemotherapy. The last line of chemotherapy should have included platinum.

- Availability at the study site of a representative FFPE tumor sample or at least 15 unstained slides from debulking surgery during front-line therapy

- ECOG performance status 0-1

EXCLUSION CRITERIA

- Non-epithelial tumor origin of the ovary, the fallopian tube or the peritoneum (i.e. germ cell tumors)
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, anti-PD1, or anti-PDL1 therapeutic antibodies or anti-CTLA 4
- Treatment with systemic corticosteroids or other systemic immunosuppressive medications within 2 weeks prior to Cycle 1Day 1, or anticipated requirement for systemic immunosuppressive medications during the trial
- History of autoimmune disease
- Treatment with systemic immunostimulatory agents within 4 weeks or five half-lives of the drug prior to Cycle 1Day 1
- Immunocompromised patients, e.g., patients who are known to be serologically positive for human immunodeficiency virus (HIV)
- Current or recent (within 10 days prior to randomization) chronic use of aspirin > 325 mg/day
- Inadequately controlled HTN
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.

STUDY CHARACTERISTICS

- Fresh biopsy mandatory at screening for PD-L1 status
- Archived tissue required at screening
- Questionnaires of quality of life to be collected until PFS2
- Mandatory scanners at week 12, 24, 48, 72; 96
- One additional scanner 4 weeks after the scanner of PD