ATALANTE: Atezolizumab vs Placebo Phase III Study in Late Relapse Ovarian Cancer Treated With Chemotherapy+Bevacizumab (ATALANTE)

ClinicalTrials.gov Identifier: NCT02891824

Recruitment Status: Recruiting
First Posted: September 8, 2016
Last Update Posted: November 14, 2018
See Contacts and Locations

Sponsor:
ARCAGY/ GINECO GROUP

Collaborator:
Hoffmann-La Roche

Information provided by (Responsible Party):
ARCAGY/ GINECO GROUP

Brief Summary:

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.
This is a phase III, randomized, double-blinded, comparative, multi-centre study to assess the efficacy of atezolizumab in combination with platinum-based chemotherapy plus bevacizumab administered concurrent to chemotherapy and in maintenance, in patients presenting epithelial ovarian cancer (including patients with primary peritoneal and / or fallopian tube adenocarcinoma) who have platinum-sensitive relapse (platinum-free interval > 6 months).

<table>
<thead>
<tr>
<th>Condition or disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Cancer</td>
<td>Drug: atezolizumab + avastin + platinum-based chemotherapy</td>
<td>Phase 3</td>
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<tr>
<td></td>
<td>Drug: placebo + avastin + platinum-based chemotherapy</td>
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Detailed Description:

Approximately 405 patients will be randomized using an Interactive Voice Response System /Interactive web system (IVR/IWR system) in a 1:2 ratio to the treatments as specified below:

A. Arm A: Placebo + bevacizumab & platinum-based chemotherapy.

The placebo arm will include one of 3 following regimens up to investigator choice (chosen prior to randomization)

1. Carboplatin (day1) combined with gemcitabine (day1 & day8) and bevacizumab (day1) + placebo (day1) x 6 cycles q3weeks followed by maintenance with bevacizumab (day1) + placebo (day1) q3weeks until disease progression or

2. Carboplatin (d1) combined with paclitaxel (day1) and bevacizumab (day1) + placebo (d1) x 6 cycles every 3weeks followed by maintenance with bevacizumab (day1) + placebo (day1) q3weeks until disease progression or

3. Carboplatin (day1) combined with pegylated liposomal doxorubicin (PLD) (day1) and bevacizumab (day1 & 15) + placebo (day1& 15) x 6 cycles every 4weeks followed by maintenance with bevacizumab (day1) + placebo (day1) q3weeks until disease progression.

B. Arm B: Atezolizumab + bevacizumab & platinum-based chemotherapy

The atezolizumab arm will include one of 3 following regimens up to investigator choice (chosen prior to randomization)

1. Carboplatin (day1) combined with gemcitabine (day1 & d8) and bevacizumab (day1) + atezolizumab (day1) x 6 cycles q3weeks followed by maintenance with bevacizumab (day1) + atezolizumab (day1) q3w until disease progression or

2. Carboplatin (day1) combined with paclitaxel (day1) and bevacizumab (day1) + atezolizumab (1200mg, d1) x 6 cycles every 3wk (day1) q3weeks until disease progression or

3. Carboplatin (day1) combined with pegylated liposomal doxorubicin (PLD) (day1) and bevacizumab (day1 & 15) + atezolizumab (day1& 15) x 6 cycles every 4weeks followed by maintenance with bevacizumab (day1) + atezolizumab (day1) q3weeks until disease progression.
Before randomization to the study:

- A tumor biopsy should have been obtained and sent to the central laboratory
- PD-L1 status should be determined

**Study Design**

**Study Type**: Interventional (Clinical Trial)

**Estimated Enrollment**: 405 participants

**Allocation**: Randomized

**Intervention Model**: Parallel Assignment

**Masking**: Triple (Participant, Care Provider, Investigator)

**Primary Purpose**: Treatment

**Official Title**: 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

**Study Start Date**: September 2016

**Estimated Primary Completion Date**: September 2020

**Estimated Study Completion Date**: September 2023

**Resource links provided by the National Library of Medicine**

- Genetics Home Reference related topics: Ovarian cancer
- MedlinePlus related topics: Ovarian Cancer
- Drug Information available for: Atezolizumab
- Genetic and Rare Diseases Information Center resources: Ovarian Cancer, Ovarian Epithelial Cancer
- U.S. FDA Resources

**Arms and Interventions**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Intervention/treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo Comparator: Arm A: Placebo + Avastin + platinum-based chemotherapy</td>
<td>Drug: placebo + avastin + platinum-based chemotherapy</td>
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<tr>
<td>The placebo arm:</td>
<td>placebo will be administrated by intravenous route</td>
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<tr>
<td>Placebo 1200 mg x 6 cycles q3wk or</td>
<td>at dose of 1200 mg or 800 mg during the induction</td>
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<tr>
<td>800mg x 6 cycles q4wk during treatment</td>
<td>period and will be continued in maintenance period</td>
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<tr>
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<td>at a dose of 1200mg until progression</td>
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with chemotherapy and Avastin, followed by placebo 1200mg q3wk until progression

- avastin will be administered by intravenous route at dose of 15mg/kg or 10 mg/kg during the induction period and will be continued in maintenance period of at a dose of 15mg/kg until progression
- platinum-based chemotherapy (Carboplatin combined with gemcitabine or paclitaxel or pegylated liposomal doxorubicin) will be administered by intravenous route at different doses during the induction period x 6 cycles

Drug: atezolizumab + avastin + platinum-based chemotherapy

- atezolizumab will be administered by intravenous route at dose of 1200 mg or 800 mg during the induction period and will be continued in maintenance period at a dose of 1200mg until progression
- avastin will be administered by intravenous route at dose of 15mg/kg or 10 mg/kg during the induction period and will be continued in maintenance period of at a dose of 15mg/kg until progression
- platinum-based chemotherapy (Carboplatin combined with gemcitabine or paclitaxel or pegylated liposomal doxorubicin) will be administered by intravenous route at different doses during the induction period x 6 cycles

Other Name: Tecentriq

### Outcome Measures

**Primary Outcome Measures**

1. Efficacy: Progression free survival, where the date of progression is based on investigator assessment using the RECIST version 1.1 [ Time Frame: An average of 19 months ]

**Secondary Outcome Measures**

1. Efficacy: Time from date randomization to second subsequent therapy or date of death (TSST)
whichever come first [ Time Frame: To be assessed around 73 months ]

2. Efficacy: Overall survival (OS) [ Time Frame: To be assessed around 73 months ]

3. patient reported outcome variables [ Time Frame: to be assessed 19 months ]
   questionnaire to be completed by patients and collected frequently during the study

4. Adverse events [ Time Frame: to be assessed 19 months ]
   frequency of adverse events according to MedRA terms

### Eligibility Criteria

**Information from the National Library of Medicine**

*Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.*

**Ages Eligible for Study:** 18 Years to 95 Years (Adult, Older Adult)

**Sexes Eligible for Study:** Female

**Accepts Healthy Volunteers:** No

**Criteria**

**Inclusion Criteria:**

1. Female Patients must be ≥18 years of age.

2. Signed informed consent and ability to comply with treatment and follow-up.

3. Patients with histologically confirmed progressive non-mucinous epithelial ovarian cancer, primary peritoneal adenocarcinoma and / or fallopian-tube adenocarcinoma

4. Patients with PD-L1 status determined for stratification on mandatory de novo biopsy sent to central laboratory as a formalin-fixed, paraffin-embedded (FFPE) sample.
   - Cell pellet from pleural effusion, or ascites or lavage are not acceptable.
   - For core needle biopsy specimens, at least three cores should be obtained. Biopsies must be obtained in a manner that minimizes risks. If the location of the tumor renders tumor biopsy medically unsafe or not feasible, patient eligibility should be discussed with the sponsor.

5. Patients whose disease has relapsed more than 6 months from the last dose of platinum before randomization:
   1. criterion for relapse can be according to RECIST v1.1, CA-125 (GCIG) or clinical symptoms
2. the interval between last dose of platinum and entry in the study should be free of new anti-
cancer treatment, with the exception of a maintenance therapy which is allowed up to 21 days
before study entry.

6. Patients with one or 2 prior lines of chemotherapy. The last line of chemotherapy should have
included platinum.

7. Availability at the study site of representative FFPE tumor sample from surgery during front line
therapy, at best before chemotherapy

8. Patients must have normal organ and bone marrow function:
   1. Haemoglobin ≥ 10.0 g/dL.
   2. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L.
   3. Platelet count ≥ 100 x 109/L.
   4. Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN).
   5. Aspartate aminotransferase /Serum Glutamic Oxaloacetic Transaminase (ASAT/SGOT)) and
      Alanine aminotransferase /Serum Glutamic Pyruvate Transaminase (ALAT/SGPT)) ≤ 2.5 x
      ULN, unless liver metastases are present in which case they must be ≤ 5 x ULN.
   6. Serum creatinine ≤ 1.5 x institutional ULN,
   7. Patients not receiving anticoagulant medication who have an International Normalized Ratio
      (INR) ≤1.5 and an Activated ProThrombin Time (aPTT) ≤1.5 x ULN. The use of full-dose oral or
      parenteral anticoagulants is permitted as long as the INR or APTT is within therapeutic limits
      (according to site medical standard) and if the patient is on a stable dose of anticoagulants for
      at least two weeks at the time of randomization.
   8. Urine dipstick for proteinuria < 2+. If urine dipstick is ≥2+, 24-hours urine must demonstrate ≤1
      g of protein in 24 hours.
   9. Normal blood pressure or adequately treated and controlled hypertension (systolic BP ≤ 140
      mmHg and/or diastolic BP ≤ 90 mmHg).

9. Eastern Cooperative Oncology Group (ECOG) performance status 0-1

For France only: In France, a subject will be eligible for randomization in this study only if either affiliated to,
or a beneficiary of, a social security category

Exclusion Criteria:

1. Non-epithelial tumor origin of the ovary, the fallopian tube or the peritoneum (i.e. germ cell tumors).
2. Ovarian tumors of low malignant potential (e.g. borderline tumors)
3. Patients with synchronous primary endometrial cancer unless both of the following criteria are met:
   1. stage < II,
   2. Less than 60 years old at the time of diagnosis of endometrial cancer with stage IA or IB grade
      1 or 2, or stage IA grade 3 endometrioid adenocarcinoma OR ≥ 60 years old at the time of
      diagnosis of endometrial cancer with stage IA grade 1or 2 endometrioid adenocarcinoma.
   3. Patients with serous or clear cell adenocarcinoma or carcinosarcoma of the endometrium are
      not eligible.
4. Other malignancy within the last 5 years except cervix or breast in situ carcinoma, breast cancer ≥ 3 years free of disease and treatment, type I stage I endometrial cancer.
5. Patients receiving radiotherapy within 6 weeks prior to study treatment.
6. Major surgery within 4 weeks of starting study treatment or patients who have not completely recovered from the effects of any major surgery. Core biopsy or other minor surgical procedure, excluding placement of a vascular access device, within 7 days prior to Day 1, Cycle 1
7. Previous allogeneic bone marrow transplant or previous solid organ transplantation.
8. Administration of other simultaneous chemotherapy drugs, any other anticancer therapy or antineoplastic hormonal therapy, or simultaneous radiotherapy during the trial treatment period (hormonal replacement therapy is permitted).
9. Prior treatment with CD137 agonists or immune checkpoint blockade therapies, anti–PD1, or anti–PDL1 therapeutic antibodies or anti-CTLA 4.
10. Treatment with systemic immunostimulatory agents (including but not limited to interferon-alpha (IFN-α) and interleukin-2 (IL-2) within 4 weeks or five half-lives of the drug (whichever is shorter) prior to Cycle 1, Day 1
11. Treatment with systemic corticosteroids or other systemic immunosuppressive medications (including but not limited to prednisone, dexamethasone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti–tumor necrosis factor [TNF] agents) within 2 weeks prior to Cycle 1, Day 1, or anticipated requirement for systemic immunosuppressive medications during the trial
   1. The use of inhaled corticosteroids for chronic obstructive pulmonary disease, mineralocorticoids (e.g., fludrocortisone) for patients with orthostatic hypotension, and low-dose supplemental corticosteroids for adrenocortical insufficiency are allowed.
   2. Prophylactic anti-emetic corticosteroids will be avoided if possible in patients treated with pegylated liposomal doxorubicin-carboplatin or gemcitabine-carboplatin regimen. The use of corticosteroids is allowed as premedication for paclitaxel-based regimen and/or premedication in case of carboplatin hypersensitivity.
12. History of autoimmune disease, including but not limited to myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with anti-phospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis. Are eligible patients with:
   1. a history of autoimmune hypothyroidism on a stable dose of thyroid replacement hormone
   2. controlled Type 1 diabetes mellitus on a stable insulin regimen
13. History of idiopathic pulmonary fibrosis (including pneumonitis), drug-induced pneumonitis, organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia), or evidence of active pneumonitis. Radiation pneumonitis in the radiation field (fibrosis) detected on screening chest CT scan is permitted
14. Immunocompromised patients, e.g., patients who are known to be serologically positive for human immunodeficiency virus (HIV). Patients with active hepatitis B (defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C.
Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as having a negative HBsAg test and a positive antibody to hepatitis B core antigen [anti-HBc] antibody test) are eligible. Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction (PCR) is negative for HCV RNA.

15. Signs or symptoms of infection within 2 weeks prior to Cycle 1, Day 1

16. Administration of a live, attenuated vaccine within 4 weeks prior to Cycle 1, Day 1 or anticipation that such a live attenuated vaccine will be required during the study. Influenza vaccination should be given during influenza season only (example approximately October to March in the Northern Hemisphere). Patients must not receive live, attenuated influenza.

17. Current or recent (within 10 days prior to randomization) chronic use of aspirin > 325 mg/day.

18. Prior history of hypertensive crisis (CTC-AE grade 4) or hypertensive encephalopathy.

19. Inadequately controlled HTN (defined as systolic blood pressure > 150 mmHg and/or diastolic blood pressure > 100 mmHg on antihypertensive medications)

20. Clinically significant (e.g. active) cardiovascular disease, including:
   1. Myocardial infarction or unstable angina within ≤ 6 months of randomization,
   2. New York Heart Association (NYHA) ≥ grade 2 congestive heart failure (CHF),
   3. Poorly controlled cardiac arrhythmia despite medication (patients with rate controlled atrial fibrillation are eligible),
   4. Peripheral vascular disease grade ≥ 3 (e.g. symptomatic and interfering with activities of daily living [ADL] requiring repair or revision)

21. Resting ECG with QTc > 470 msec on 2 or more time points within a 24 hour period or family history of long QT syndrome.

22. Left ventricular ejection fraction defined by MUGA/ECHO below the institutional lower limit of normal (only applicable for patients intended to be treated with pegylated liposomal doxorubicin).

23. Previous Cerebro-Vascular Accident (CVA), Transient Ischemic Attack (TIA) or Sub-Arachnoids Hemorrhage (SAH) within 6 months prior to randomization.

24. History or evidence of hemorrhagic disorders within 6 months prior to randomization.

25. Evidence of bleeding diathesis or significant coagulopathy (in the absence of coagulation).

26. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory (within 4 weeks prior to randomization) in case of suspected brain metastases. Spinal MRI is mandatory (within 4 weeks prior to randomization) in case of suspected spinal cord compression.

27. History or evidence upon neurological examination of central nervous system (CNS) disease, unless adequately treated with standard medical therapy (e.g. uncontrolled seizures).

28. Significant traumatic injury during 4 weeks prior to randomization.

29. Non-healing wound, active ulcer or bone fracture. Patients with granulating incisions healing by secondary intention with no evidence of facial dehiscence or infection are eligible but require 3 weekly wound examinations.

30. History of VEGF therapy related abdominal fistula or gastrointestinal perforation.
31. Current, clinically relevant bowel obstruction, including sub-occlusive disease, related to underlying disease.

32. Patients with evidence of abdominal free air not explained by paracentesis or recent surgical procedure.

33. Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment related complications.

34. Women of childbearing potential (<2 years after last menstruation and not surgically sterile) not willing to use highly-effective means of contraception (Appendix 1) during the study and for 6 months after the last dose of study medication

35. Pregnant or lactating women.

36. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.

37. Known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cells or to any component of the atezolizumab formulation.

38. Known hypersensitivity reaction or allergy to drugs chemically related to bevacizumab, carboplatin, gemcitabine, paclitaxel, pegylated liposomal doxorubicin, or their excipients that contraindicates the subject’s participation.
**Principal Investigator:** Jean-Emmanuel KURTZ  
**GINECO - Hôpitaux Universitaires de Strasbourg**

### More Information

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<thead>
<tr>
<th>Responsible Party:</th>
<th>ARCAGY/ GINECO GROUP</th>
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| ClinicalTrials.gov Identifier: | [NCT02891824](https://clinicaltrials.gov/ct2/show/NCT02891824)  
[History of Changes](https://clinicaltrials.gov/ct2/show/NCT02891824) |
| Other Study ID Numbers: | GINECO-OV236b |
| First Posted: | September 8, 2016  
[Key Record Dates](https://clinicaltrials.gov/ct2/show/NCT02891824) |
| Last Update Posted: | November 14, 2018 |
| Last Verified: | November 2018 |

**Keywords provided by ARCAGY/ GINECO GROUP:**

- **PD-L1**  
  first or second late relapse
- **Atezolizumab**  
  progressive non-mucinous epithelial ovarian cancer, primary peritoneal
- **Randomized, double blinded**  
  adenocarcinoma and / or fallopian-tube adenocarcinoma  
  progression-free survival

**Additional relevant MeSH terms:**

- **Ovarian Neoplasms**  
  Neoplasms by Histologic Type
- **Carcinoma, Ovarian Epithelial**  
  Disease Attributes
- **Recurrence**  
  Pathologic Processes
- **Endocrine Gland Neoplasms**  
  Bevacizumab
- **Neoplasms by Site**  
  Atezolizumab
- **Neoplasms**  
  Liposomal doxorubicin
- **Ovarian Diseases**  
  Doxorubicin
- **Adnexal Diseases**  
  Antibodies, Monoclonal
- **Genital Diseases, Female**  
  Antineoplastic Agents, Immunological
- **Genital Neoplasms, Female**  
  Antineoplastic Agents
- **Urogenital Neoplasms**  
  Angiogenesis Inhibitors
- **Endocrine System Diseases**  
  Angiogenesis Modulating Agents
- **Gonadal Disorders**  
  Growth Substances
- **Carcinoma**  
  Physiological Effects of Drugs
- **Neoplasms, Glandular and Epithelial**  
  Growth Inhibitors