

KURZPROTOKOLL **AGO Ovar 2.29**

Öffentlicher Titel	Phase III Studie zu Atezolizumab beim rezidivierendem Ovarialkarzinom
Wissenschaftl. Titel	Atezolizumab in Kombination mit Bevacizumab und Chemotherapie versus Bevacizumab und Chemotherapie beim rezidivierendem Ovarialkarzinom – eine randomisierte Phase III-Studie.
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Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase III
Erkrankung	Geschlechtsorgane: Krebserkrankungen der weiblichen Geschlechtsorgane: Eierstockkrebs (Ovarialkarzinom) - Zweitlinie oder höher
Einschlusskriterien	<ul style="list-style-type: none">- Patients with histologically diagnosed ovarian, fallopian tube, or primary peritoneal cancer- Relapsed disease- Patients with up to three prior therapies. In patients with 1 or 2 prior treatment lines, the treatment free interval after platinum has to be less than 6 months; in addition patients with three prior lines of chemotherapy who are not considered for platinum-containing chemotherapy lines are also eligible- Measurable disease, evaluable disease in combination with GCIG CA-125 criteria, or histologically proven relapse/progression- Patient agrees and is able to provide a recent tumor biopsy (not older than 3 months) or agrees and has a tumor lesion amenable for taking a new tumor biopsy.- Availability of a representative archival FFPE tumor sample (preferable from primary diagnosis)- Patient has not progressed on the chosen/planned chemotherapy (PLD or Paclitaxel) in any prior line- Patients previously treated with bevacizumab are eligible, with the exclusion of those patients that has suspended bevacizumab for more than 2 subsequent cycles or permanently discontinued bevacizumab during their previous treatment due to toxicity. A washout period of at least 20 days after last bevacizumab treatment must be adhered.- Females aged ≥ 18 years at signing at time of signing informed consent form- Signed written informed consent and ability to comply with the study protocol, in the investigator's judgement- Adequate hematological, renal and hepatic function within 28 days prior to first administration of study treatment:<ul style="list-style-type: none">1. Hemoglobin ≥ 9.0 g/dl2. Absolute neutrophil count (ANC) $\geq 1.5 \times 10^9/L$3. Platelet count $\geq 100 \times 10^9/L$4. Total bilirubin $\leq 1.5 \times$ institutional upper limit of normal (ULN)5. Aspartate aminotransferase /Serum Glutamic Oxaloacetic Transaminase (ASAT/SGOT) and Alanine aminotransferase /Serum Glutamic Pyruvate Transaminase (ALAT/SGPT) $\leq 2.5 \times$ ULN, unless liver metastases are present, in case of liver metastases values must be $\leq 5 \times$ ULN6. Serum creatinine $\leq 1.5 \times$ institutional ULN7. Patient not receiving anticoagulant medication who has an International Normalized Ratio (INR) ≤ 1.5 and an Activated ProThrombin Time (aPTT) $\leq 1.5 \times$ 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). If the patient is on oral anticoagulants, dose has to be stable for at least two weeks at the time of randomization

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- 8. Urine dipstick for proteinuria < 2+. If urine dipstick is \geq 2+, 24-hours urine must demonstrate \leq 1 g of protein in 24 hours.
- Patients must have adequately controlled blood pressure (BP), with a systolic BP of \leq 140 mmHg and diastolic BP of \leq 90 mmHg for eligibility. Patients must have a BP of \leq 140/90 mmHg taken in the clinic setting by a medical professional within 2 weeks prior to starting study.
- Estimated life expectancy of at least 3 months
- ECOG performance status 0 – 1
- Negative urine or serum pregnancy test within 7 days of study treatment in women of childbearing potential (WOCBP), confirmed prior to treatment on day 1
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual inter-course) or use a contraceptive method with a failure rate of < 1% per year during the treatment period and for at least 5 months after administration of the last dose of atezolizumab/placebo and 6 months after the last dose of bevacizumab, paclitaxel, or PLD, whichever is later.
- For countries where this will apply to: a patient will be eligible for randomization in this study only, if either affiliated to, or a beneficiary of a social security category.
- Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures, that include the completion of patient-reported outcomes questionnaires.

Ausschlusskriterien

- Non-epithelial tumor origin of the ovary, the fallopian tube or the peritoneum
- Ovarian tumors of low malignant potential
- Malignancies other than ovarian cancer within 5 years prior to randomisation.
- More than three prior systemic anticancer regimens; maintenance therapies are not calculated as separate line.
- Prior systemic anticancer therapy within 28 days before randomization.
- Prior radiotherapy to the pelvis or the abdomen.
- Administration of other simultaneous chemotherapy drugs, any other anticancer therapy or anti-neoplastic hormonal therapy, or simultaneous radiotherapy during the trial treatment period.
- Prior treatment with anti-CD137 or immune checkpoint blockade therapies, anti-PD1, or anti-PD-L1 therapeutic antibodies or anti-CTLA 4
- Prior randomization in AGO-OVAR 2.29.
- Treatment with systemic immunostimulatory agents (including but not limited to interferon-alpha and interleukin-2 within 4 weeks or five half-lives of the drug (whichever is longer) prior to Cycle 1, Day 1
- Treatment with systemic corticosteroids or other systemic immunosuppressive medications within 2 weeks prior to Cycle 1, Day 1, or anticipated requirement for systemic immunosuppressive medications during the trial. The use of inhaled corticosteroids for chronic obstructive pulmonary disease, mineral-corticoids.
- Patients with a history of allergic reaction to IV contrast requiring steroid pre-treatment should have screening and subsequent tumor assessments performed using MRI.
- 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 or within 5 months after the last dose of atezolizumab/placebo.
- Major surgery within 4 weeks of starting study treatment or patient who has not completely recovered from the effects of any major surgery. Core biopsy or other minor surgical procedure within 7 days prior to day 1, cycle 1 is permitted.
- Previous allogeneic bone marrow transplant or previous solid organ transplantation.

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- Current treatment with anti-viral therapy for HBV.
- History of idiopathic pulmonary fibrosis (including pneumonitis), organizing pneumonia, or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) detected on screening chest CT scan is permitted
- Previous Cerebro-Vascular Accident, Transient Ischemic Attack or Sub-Arachnoids Hemorrhage within 6 months prior to randomization
- History or evidence of thrombotic or hemorrhagic disorders within 6 months prior to randomization
- History or clinical suspicion of brain metastases or spinal cord compression.
- History of autoimmune disease
- Any prior history of hypertensive crisis (CTCAE grade 4) or hypertensive encephalopathy
- Immunocompromised patients
- Persistent toxicities (\geq CTCAE grade 2)
- Severe infection requiring oral or IV antibiotics within 4 weeks prior to randomization
- Current or recent (within 10 days prior randomization) chronic use of aspirin $>$ 325 mg/day
- Clinically significant cardiovascular disease
- For patients with PLD treatment: Left ventricular ejection fraction defined by ECHO below the institutional lower limit of normal
- Evidence of bleeding diathesis or significant coagulopathy
- Non-healing wound, active ulcer or bone fracture
- History of bowel obstruction related to underlying disease, a history of abdominal fistula, GI perforation, or intra-abdominal abscess, or evidence of deep infiltration of the bowel by pelvic examination or on computed tomography, or clinical symptoms of bowel obstruction
- Patients with evidence of abdominal free air
- Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment related complications
- Known hypersensitivity or allergy to drugs containing Chinese hamster (CHO) ovary cells or history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity reaction or allergy to drugs chemically related to bevacizumab, paclitaxel, pegylated liposomal doxorubicin, or their excipients that contraindicates the subject's participation.
- Patients considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection. This includes also any psychiatric disorder that prohibits obtaining informed consent.
- Pregnancy, lactation, or intention to become pregnant during the study or within 5 months after the last dose of atezolizumab/placebo.

Alter
Status

18 Jahre und älter
Aktiv

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Sponsor

Roche Pharma AG
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**Registrierung in anderen
Studienregistern**

ClinicalTrials.gov NCT03353831 (primäres Register)
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Links

[Studiendokumente zum Download](#)