KURZPROTOKOLL
GeparOLA

Öffentlicher Titel	Randomisierte Phase II Studie zu Paclitaxel plus Olaparib als neoadjuvante Therapie bei HER2-negativem Brustkrebs
Wissenschaftl. Titel	Eine randomisierte Phase II-Studie zum Vergleich von Paclitaxel/Olaparib versus Paclitaxel / Carboplatin gefolgt von Epirubicin / Cyclophosphamid als neoadjuvante Behandlung von Patienten mit HER2-negativem primären Brustkrebs mit homologen rekombinanten Mangel (HRD) [HRD Patienten mit abträglichen Tumor oder Keimbahn BRCA 1/2 Mutationen und / oder HRD-Score hoch] (GeparOLA)
Kurztitel	GeparOLA
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Geschlechtsorgane: Brustkrebs: neoadjuvant
Einschlusskriterien	- Written informed consent for all study specific procedures according to local regulatory requirements prior to beginning specific protocol procedures. - Complete baseline documentation must be sent to GBG Forschungs GmbH. - Unilateral or bilateral primary carcinoma of the breast, confirmed histologically by core biopsy. Fine-needle aspiration alone is not sufficient. Incisional biopsy is not allowed. In case of bilateral cancer, the investigator has to decide prospectively which side will be evaluated for the primary endpoint. - Centrally confirmed negative HER2-status. Centrally confirmed estrogen and progesterone receptor, and Ki-67 status detected on core biopsy. ER/PR positive is defined as >=1% stained cells and HER2-positive is defined as IHC 3+ or in-situ hybridisation (ISH) ratio >=2.0. Formalin-fixed, paraffin-embedded (FFPE) breast tissue from core biopsy has therefore to be sent to the Dept. of Pathology at the Charité, Berlin prior to randomization. - Centrally confirmed tumor Homologous Recombinant Deficiency score (tBRCA positive/mutated and/or HRD high). Patients with known gBRCA and/or tBRCA status can be enrolled prior to the central test results available. - Tumor lesion in the breast with a palpable size of >= 2 cm or a sonographical size of >= 1 cm in maximum diameter. If the tumor is not detectable with sonography mammography assessment can be considered. The lesion has to be measurable in two dimensions, preferably by sonography. In case of inflammatory disease, the extent of inflammation can be used as measurable lesion. - Patients must be in the following stages of disease: (a) cT2 - cT4a-d or; (b) cT1c and cN+ or cT1c and pNSLN+ or; (c) cT1c and ER-neg and PR-neg or; (d) cT1c and Ki67>20% - In patients with multifocal or multicentric breast cancer, the largest lesion should be measured and at least one lesion has to meet the above criteria - Age >= 18 years - Karnofsky Performance status index >= 80%. - Normal cardiac function must be confirmed by ECG and cardiac ultrasound (LVEF or shortening fraction) within 3 months prior to randomization. Results must be above the normal limit of the institution. - aboratory requirements: (a) Absolute neutrophil count (ANC) >= 2.0 x 109 / L and - Platelets >= 100 x 109 / L and - Hemoglobin >= 10 g/dL (>= 6.2 mmol/L); (b) Total bilirubin 1.5x UNL and - ASAT (SGOT) and ALAT (SGPT) 1.5x UNL and - Alkaline phosphatase 2.5x UNL. - Negative pregnancy test (urine or serum) within 14 days prior to randomization for all women of childbearing potential.

	- Complete staging work-up within 3 months prior to randomization. All patients must have bilateral mammography, breast ultrasound (<= 21 days, and in no case exceed 6 weeks prior to randomization) (Note MRI/ CT scan may be used as an alternative imaging technique). In case of high risk according to guidelines: chest X-ray (PA and lateral) or as an alternative breast MRI/CT, abdominal ultrasound or CT scan or MRI, and bone scan in case of high risk for primary metastasis according to guidelines. In case of positive bone scan, bone X-ray or CT scan is mandatory. Other tests may be performed as clinically indicated. - Male or female patients - Patients must be available and compliant for central diagnostics, treatment and follow -up.
Ausschlusskriterien	- Prior chemotherapy for any malignancy within 5 years. - Prior radiation therapy for breast cancer within 5 years. - Pregnant or lactating patients. Patients of childbearing potential must implement adequate non-hormonal contraceptive measures (barrier methods, intrauterine contraceptive devices, sterilization) during study treatment. - Inadequate general condition (not fit for anthracycline-taxane-targeted agents-based chemotherapy). - Previous malignant disease without being disease-free for less than 5 years (except CIS of the cervix and non-melanomatous skin cancer). - Known or suspected congestive heart failure (>NYHA I) and / or coronary heart disease, angina pectoris requiring antianginal medication, previous history of myocardial infarction, evidence of transmural infarction on ECG, uncontrolled or poorly controlled arterial hypertension (i.e. BP >140 / 90 mm Hg under treatment with two antihypertensive drugs), rhythm abnormalities requiring permanent treatment, clinically significant valvular heart disease. - History of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent. - Patients currently in an institution by order of jurisdictional or governmental grounds. - Currently active infection. - Definite contraindications for the use of corticosteroids. - Known hypersensitivity reaction to one of the compounds or incorporated substances used in this protocol. - Concurrent treatment with: (a) chronic corticosteroids unless initiated > 6 months prior to study entry and at low dose (10 mg or less methylprednisolone or equivalent); (b) sex hormones. Prior treatment must be stopped before study entry; (c) other experimental drugs or any other anti-cancer therapy. - Participation in another clinical trial with any investigational, not marketed drug within 30 days prior to study entry. - Prior use of a PARP-Inhibitor
Alter	18 Jahre und älter
Molekularer Marker	BRCA HER2/neu neg./ER pos. HER2/neu neg./PR pos.
Sponsor	German Breast Group
Förderer	Astra Zeneca
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02789332 EudraCT 2015-003509-41