

This site became the new [ClinicalTrials.gov](#) on June 19th. [Learn more.](#)

We will be updating this site in phases. This allows us to move faster and to deliver better services.

[Show less](#)

▲ IMPORTANT: Listing of a study on this site does not reflect endorsement by the National Institutes of Health. Talk with a trusted healthcare professional before volunteering for a study. [Read more...](#)

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Saved Studies (0)

[Give us feedback](#)

Trial record **1 of 1** for: **GeparOla**

[Previous Study](#) | [Return to List](#) | [Next Study](#)

Assessing the Efficacy of Paclitaxel and Olaparib in Comparison to Paclitaxel / Carboplatin Followed by Epirubicin/Cyclophosphamide as Neoadjuvant Chemotherapy in Patients With HER2-negative Early Breast Cancer and Homologous Recombination Deficiency (GeparOla)

This study is currently recruiting participants.

See [▶ Contacts and Locations](#)

Verified June 2017 by German Breast Group

Sponsor:

German Breast Group

Collaborator:

AstraZeneca

Information provided by (Responsible Party):

German Breast Group

ClinicalTrials.gov Identifier:

NCT02789332

First received: May 23, 2016

Last updated: June 26, 2017

Last verified: June 2017

[History of Changes](#)

[Full Text View](#)

[Tabular View](#)

[No Study Results Posted](#)

[Disclaimer](#)

[How to Read a Study Record](#)

[▶ Purpose](#)

This is a multicenter, prospective, randomized, open-label phase II study evaluating the efficacy and safety of PO→EC as neoadjuvant treatment of operable and locally advanced breast cancer in patients with HR deficiency. Patients will be randomized to receive

- paclitaxel 80 mg/m² iv weekly in combination with olaparib tablets 100 mg (4X25mg) twice daily for 12 weeks (65 patients) or
- paclitaxel 80 mg/m² iv weekly in combination with carboplatin AUC 2 iv weekly for 12 weeks (37 patients) both followed by 4 cycles of epirubicin 90 mg/m² and cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks followed by surgery.

The control arm was chosen to allow direct comparison with one of the currently considered standard of care regimen.

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
Breast Cancer	Drug: PwO	Phase 2
Triple Negative Breast Neoplasms	Drug: PwCb Drug: EC	
HRpos Breast Neoplasms	Procedure: Surgery after neoadjuvant Therapy	
BRCA 1 /2 and / or HRD	Other: Stratification	

Study Type: Interventional
Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: No masking
Primary Purpose: Treatment

Official Title: A Randomized Phase II Trial to Assess the Efficacy of Paclitaxel and Olaparib in Comparison to Paclitaxel / Carboplatin Followed by Epirubicin/Cyclophosphamide as Neoadjuvant Chemotherapy in Patients With HER2-negative Early Breast Cancer and Homologous Recombination Deficiency (HRD Patients With Deleterious BRCA1/2 Tumor or Germline Mutation and/or HRD Score High)

Resource links provided by NLM:

[Genetics Home Reference](#) related topics: [breast cancer](#)

[MedlinePlus](#) related topics: [Breast Cancer](#)

[Drug Information](#) available for: [Cyclophosphamide](#) [Paclitaxel](#) [Carboplatin](#) [Epirubicin hydrochloride](#) [Epirubicin](#) [Olaparib](#)

[U.S. FDA Resources](#)

Further study details as provided by German Breast Group:

Primary Outcome Measures:

- response by pCR =ypT0/is ypN0 [Time Frame: 24 weeks]

Assess the efficacy of olaparib in HER2-negative early Breast Cancer and HRD (BRCA 1/2 mutations and/or HRD positive). Pathological complete response of breast and lymph nodes (ypT0/is ypN0) defined as no microscopic evidence of residual invasive viable tumor cells in all resected specimens of the breast and axilla.

Pathological response will be assessed considering all removed breast and lymphatic tissues from all surgeries.

Secondary Outcome Measures:

- response by pCR =ypT0/is ypN0 [Time Frame: 12 weeks]

To assess the pCR rates of patients receiving PO→EC and the pCR rates of patients receiving paclitaxel and carboplatin followed by EC (PCb→EC)

- response by pCR =ypT0/is ypN0 in stratified subgroups [Time Frame: 24 weeks]

To assess the pCR rates (ypT0/is, ypN0) in the stratified subgroups

- response by pCR according to other definitions [Time Frame: 24 weeks]

To determine other pCR rates (ypT0 ypN0; ypT0 ypN0/+; ypT0/is ypN0/+; ypT(any) ypN0) of patients receiving PO→EC and to compare them with the pCR rates of patients receiving PCb→EC.

- response by pCR in HRD high versus tBRCA [Time Frame: 24 weeks]

To assess the pCR rate in HRD high with vs without tBRCA mutation

- Response rate by sono and/or mammo [Time Frame: 12 weeks]

To determine the response rates of the breast tumor and axillary nodes based on physical examination and imaging tests (sonography, mammography, or MRI) with PO→EC and to compare it with PCb→EC. Clinical (c) and imaging (i) response will be assessed after EC and before surgery by physical examination and imaging tests. Sonography is the preferred examination, however, if sonography appears not to provide valid results or is not performed, other imaging tests will be considered.

- Response rate by sono and/or mammo [Time Frame: 24 weeks]

To determine the response rates of the breast tumor and axillary nodes based on physical examination and imaging tests (sonography, mammography, or MRI) with PO→EC and to compare it with PCb→EC. Clinical (c) and imaging (i) response will be assessed after EC and before surgery by physical examination and imaging tests. Sonography is the preferred examination, however, if sonography appears not to provide valid results or is not performed, other imaging tests will be considered.

- Breast Conservation rate [Time Frame: 24 weeks]

To determine the breast conservation rate with PO→EC and to compare it with PCb→EC. Breast conservation is defined as tumorectomy, segmentectomy or quadrantectomy as a most radical surgery.

- Toxicity of treatment [Time Frame: 24 weeks]

To assess the toxicity and compliance of PO→EC and to compare it with PCb→EC. Tolerability and safety will be assessed on the basis of adverse events, serious adverse events, adverse events of special interest and treatment discontinuations. Safety by toxicity grades is defined by the NCI-CTCAE version 4.0.

Other Outcome Measures:

- Potential biomarkers predicting safety and compliance, like SNPs, TILs, PARP, 53BP1, REV7 and other biomarkers considered for breast cancer [Time Frame: 24 weeks]

To correlate co-occurring mutations detected by next generation sequencing in lymphocytes or in tumors cells with pCR (exploratory). Blood amplifying before start of Treatment, after 12 and after 24 weeks

Estimated Enrollment: 102
Actual Study Start Date: September 2016
Estimated Study Completion Date: November 2018
Estimated Primary Completion Date: November 2018 (Final data collection date for primary outcome measure)

<u>Arms</u>	<u>Assigned Interventions</u>
<p>Active Comparator: Paclitaxel with Carboplatin (PwCb) paclitaxel 80 mg/m² iv weekly in combination with carboplatin AUC 2 iv weekly for 12 weeks (37 patients) followed by 4 cycles of epirubicin 90 mg/m² and cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks followed by surgery.</p>	<p>Drug: PwCb paclitaxel 80 mg/m² iv weekly in combination with carboplatin AUC 2 iv weekly for 12 weeks (PwCb) (37 patients) Other Name: Paclitaxel Carboplatin over 12 weeks, Control arm currently considered standard of care regimen Drug: EC both Arms followed by 4 cycles of epirubicin 90 mg/m² and cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks followed by surgery. Other Name: Epirubicin 90 mg/m² and Cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks Procedure: Surgery after neoadjuvant Therapy In both study arms, treatment will be given until surgery, disease progression, unacceptable toxicity, or withdrawal of consent of the patients. Other: Stratification Hormone-receptor status (HR+ vs HR-) Age < 40 years vs >= 40 years Other Name: Randomization will be performed using Pocock minimization method, stratified for the following criteria:</p>

Experimental: Paclitaxel with Olaparib (PwO)
paclitaxel 80 mg/m² iv weekly in combination with olaparib tablets 100 mg twice daily for 12 weeks (65 patients)
followed by 4 cycles of epirubicin 90 mg/m² and cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks followed by surgery.

Drug: PwO
paclitaxel 80 mg/m² iv weekly in combination with olaparib tablets 100 mg twice daily for 12 weeks (PwO) (65 patients)
Other Name: Paclitaxel Olaparib over 12 weeks
Drug: EC
both Arms followed by 4 cycles of epirubicin 90 mg/m² and cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks followed by surgery.
Other Name: Epirubicin 90 mg/m² and Cyclophosphamide 600 mg/m² (EC) either every 3 or every 2 weeks
Procedure: Surgery after neoadjuvant Therapy
In both study arms, treatment will be given until surgery, disease progression, unacceptable toxicity, or withdrawal of consent of the patients.
Other: Stratification
Hormone-receptor status (HR+ vs HR-)
Age < 40 years vs >= 40 years
Other Name: Randomization will be performed using Pocock minimization method, stratified for the following criteria:

Detailed Description:

The efficacy of olaparib in germline HRD score high with or without BRCA 1/2 mutation carriers with breast cancer is not well described

- The efficacy and safety of olaparib included in a standard of care regimen like paclitaxel weekly followed by epirubicin and cyclophosphamide (Pw-->EC) is unknown
- Carboplatin increased the pCR rate in patients with triple-negative breast cancer (TNBC) in two randomized phase II neoadjuvant studies when added to an anthracycline, cyclophosphamide and paclitaxel (GeparSixto, CALBG 40603). pCR rates were even higher in patients with germline BRCA 1 or 2 mutations (ypT0/is ypN0 65%) and with HRD score high (ypT0/is ypN0 63%).
- The TNT study showed a doubling in response rate for patients receiving carboplatin vs docetaxel in patients with germline BRCA 1 or 2 mutations.
- There is a high correlation between tumor and germline BRCA 1/2 mutations.
- Data from GeparSixto study showed that triple negative breast patients have an HR deficiency in about 70% (67% have a high HRD and 30% have a tBRCA mutation)
- About 5% of tBRCA patients have a low HRD score

- gBRCA2 patients are older when diagnosed and are more likely to have an HRpos tumor.
- The GeparOLA study aims to support the decision for a phase III study exploring the addition of olaparib to a Pw-->EC schedule by providing an estimate on the pCR rate in the targeted population but also by providing estimate comparison to paclitaxel and carboplatin followed by epirubicin and cyclophosphamide (PCb-->EC) as carboplatin is more and more considered a standard option of care in HR deficient patients (tBRCA 1/2 mutations and/or HRD score high).

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
 Sexes Eligible for Study: All
 Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Written informed consent for all study specific procedures according to local regulatory requirements prior to beginning specific protocol procedures.
2. Complete baseline documentation must be sent to GBG Forschungs GmbH.
3. 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.
4. 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 $\geq 1\%$ 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.
5. 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.
6. 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.
7. Patients must be in the following stages of disease:
 - cT2 - cT4a-d or
 - cT1c and cN+ or cT1c and pNSLN+ or
 - cT1c and ER-neg and PR-neg or
 - 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
8. Age > 18 years.
9. Karnofsky Performance status index $\geq 80\%$.

10. 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.
11. Laboratory requirements:
Hematology
 - Absolute neutrophil count (ANC) $\geq 2.0 \times 10^9 / L$ and
 - Platelets $\geq 100 \times 10^9 / L$ and
 - Hemoglobin ≥ 10 g/dL (≥ 6.2 mmol/L) Hepatic function
 - Total bilirubin ≥ 1.5 x UNL and
 - ASAT (SGOT) and ALAT (SGPT) ≥ 1.5 x UNL and
 - Alkaline phosphatase ≥ 2.5 x UNL.
12. Negative pregnancy test (urine or serum) within 14 days prior to randomization for all women of childbearing potential.
13. 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.
14. Male or female patients
15. Patients must be available and compliant for central diagnostics, treatment and follow-up.

Exclusion Criteria:

1. Prior chemotherapy for any malignancy within 5 years.
2. Prior radiation therapy for breast cancer within 5 years.
3. Pregnant or lactating patients. Patients of childbearing potential must implement adequate non-hormonal contraceptive measures (barrier methods, intrauterine contraceptive devices, sterilization) during study treatment.
4. Inadequate general condition (not fit for anthracycline-taxane-targeted agents-based chemotherapy).
5. Previous malignant disease without being disease-free for less than 5 years (except CIS of the cervix and non-melanomatous skin cancer).
6. 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.
7. History of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent.
8. Patients currently in an institution by order of jurisdictional or governmental grounds.
9. Currently active infection.
10. Definite contraindications for the use of corticosteroids.

11. Known hypersensitivity reaction to one of the compounds or incorporated substances used in this protocol.
12. Concurrent treatment with:
 - chronic corticosteroids unless initiated > 6 months prior to study entry and at low dose (10 mg or less methylprednisolone or equivalent).
 - sex hormones. Prior treatment must be stopped before study entry.
 - other experimental drugs or any other anti-cancer therapy.
13. Participation in another clinical trial with any investigational, not marketed drug within 30 days prior to study entry.
14. Prior use of a PARP-Inhibitor

Contacts and Locations

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, see [Learn About Clinical Studies.](#)

Please refer to this study by its ClinicalTrials.gov identifier: NCT02789332

Contacts

Contact: Ioannis Gkantiragas, PhD +49 6102 7480 ext 337 geparOla@gbg.de

Contact: Jasmin Schaefer +49 6102 7480 ext 216 geparOla@gbg.de

Locations

Germany

Kliniken Esslingen, Gynäkologie Onkologie Esslingen am Neckar, Baden-Württemberg, Germany, 73730	Not yet recruiting
Universitätsklinikum Erlangen Erlangen, Bayern, Germany, 91054	Recruiting
Onkologisches Zentrum am Rotkreuzklinikum München München, Bayern, Germany, 80638	Not yet recruiting
Elisabeth Krankenhaus Kassel, Hessen, Germany, 34117	Not yet recruiting
Klinikum Südstadt Rostock, Mecklenburg-Vorpommern, Germany, 18059	Not yet recruiting
Sana Klinikum Hameln-Pyrmont Hameln, Niedersachsen, Germany, 31785	Not yet recruiting
Gemeinschaftspraxis Hildesheim, Niedersachsen, Germany, 31134	Not yet recruiting
Marienhospital Witten Witten, Nordrhein-Westfalen, Germany, 58452	Not yet recruiting

Martin-Luther-Universität Halle Wittenberg
Halle, Sachsen Anhalt, Germany, 06120

Not yet recruiting

Johanniter-Krankenhaus Genthin-Stendal
Stendal, Sachsen-Anhalt, Germany, 39576

Not yet recruiting

SRH Wald-Klinikum Gera GmbH
Gera, Thüringen, Germany, 07548

Not yet recruiting

Praxisklinik
Berlin, Germany, 10367

Not yet recruiting

Sponsors and Collaborators

German Breast Group

AstraZeneca

Investigators

Study Chair: Sibylle O Loibl, Prof., MD Sibylle Loibl, Prof., MD ASCO, ESGO, ESMO, DKG, DGGG,



More Information

Additional Information:

[GeparOla website](#) 

Publications:

Von Minckwitz G, Timms K, Untch M, Elkin E P, Fasching P A, Schneeweiss A et al. Prediction of pathological complete response (pCR) by Homologous Recombination Deficiency (HRD) after carboplatin-containing neoadjuvant chemotherapy in patients with TNBC: Results from GeparSixto. J Clin Oncol 33, 2015 (suppl; abstr 1004)

Tutt A, Ellis P, Kilburn L et al. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer. SABCS 2014.

[Sikov WM, Berry DA, Perou CM, Singh B, Cirrincione CT, Tolaney SM, Kuzma CS, Pluard TJ, Somlo G, Port ER, Golshan M, Bellon JR, Collyar D, Hahn OM, Carey LA, Hudis CA, Winer EP. Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 \(Alliance\). J Clin Oncol. 2015 Jan 1;33\(1\):13-21. doi: 10.1200/JCO.2014.57.0572. Epub 2014 Aug 4.](#)

[von Minckwitz G, Schneeweiss A, Loibl S, Salat C, Denkert C, Rezai M, Blohmer JU, Jackisch C, Paepke S, Gerber B, Zahm DM, Kümmel S, Eidtmann H, Klare P, Huober J, Costa S, Tesch H, Hanusch C, Hilfrich J, Khandan F, Fasching PA, Sinn BV, Engels K, Mehta K, Nekljudova V, Untch M. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer \(GeparSixto; GBG 66\): a randomised phase 2 trial. Lancet Oncol. 2014 Jun;15\(7\):747-56. doi: 10.1016/S1470-2045\(14\)70160-3. Epub 2014 Apr 30.](#)

Responsible Party: German Breast Group

ClinicalTrials.gov Identifier: [NCT02789332](#) [History of Changes](#)

Other Study ID Numbers: GBG90

Study First Received: May 23, 2016

Last Updated: June 26, 2017

Keywords provided by German Breast Group:

carboplatin	hormonreceptor-positive
olaparib	BRCA1/2
pCR	HRD, homologous recominant deficient
neoadjuvant	breast cancer
triple-negative	genetic testing (somatic and germline mutations)

Additional relevant MeSH terms:

Breast Neoplasms	Antimitotic Agents
Neoplasms	Mitosis Modulators
Triple Negative Breast Neoplasms	Molecular Mechanisms of Pharmacological Action
Neoplasms by Site	Immunosuppressive Agents
Breast Diseases	Immunologic Factors
Skin Diseases	Physiological Effects of Drugs
Paclitaxel	Antirheumatic Agents
Olaparib	Antineoplastic Agents, Alkylating
Albumin-Bound Paclitaxel	Alkylating Agents
Cyclophosphamide	Myeloablative Agonists
Carboplatin	Antibiotics, Antineoplastic
Epirubicin	Topoisomerase II Inhibitors
Antineoplastic Agents, Phytogetic	Topoisomerase Inhibitors
Antineoplastic Agents	Enzyme Inhibitors
Tubulin Modulators	Poly(ADP-ribose) Polymerase Inhibitors

ClinicalTrials.gov processed this record on August 04, 2017