Trial record **1 of 1** for: GeparX

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Denosumab as an add-on Neoadjuvant Treatment (GeparX) (GeparX)

This study is currently recruiting participants.

See Contacts and Locations

Verified February 2017 by German Breast Group

Sponsor:
German Breast Group

Collaborators:
Amgen
Celgene Corporation

Information provided by (Responsible Party):
German Breast Group

ClinicalTrials.gov Identifier:
NCT02682693

First received: January 27, 2016
Last updated: July 10, 2017
Last verified: February 2017
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer

How to Read a Study Record

Purpose

Pharmacologic inhibition of RANKL attenuates the development of mammary carcinoma and inhibits metastatic progression in multiple mouse models.

In a retrospective analysis it could be demonstrated that elevated expression of RANK was found in 14.5% of patients overall, with a significant predominance in patients with hormone-receptor-negative disease. Expression of RANK was associated with a higher pathological complete response rate but with a shorter disease-free and overall survival. The ABCSG-18 study showed that adjuvant denosumab reduces clinical fractures, improves bone health, and can be administered without added toxicity.

It appears therefore reasonable to test denosumab, a clinically available antibody against RANKL in patients with hormone-receptor-negative primary breast cancer as an adjunct to neoadjuvant chemotherapy for its ability to increase pCR rate and improve outcome in relation to the expression of RANK.

Condition	Intervention	Phase
Breast Cancer Female NOS Tubular Breast Cancer Stage II Mucinous Breast Cancer Stage II Invasive Ductal Breast Cancer HER2 Positive Breast Cancer Inflammatory Breast Cancer Tubular Breast Cancer Stage III	Drug: Denosumab Drug: nab-Paclitaxel Drug: Epirubicin Drug: Cyclophosphamide Drug: Carboplatin Drug: Trastuzumab Drug: Pertuzumab	Phase 2

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

Official Title: Investigating Denosumab as an add-on Neoadjuvant Treatment for RANK-positive or RANK-negative Primary Breast Cancer and Two Different Nab-Paclitaxel Schedules ; 2x2 Factorial Design (**GeparX**)

Resource links provided by NLM:

Genetics Home Reference related topics: breast cancer

MedlinePlus related topics: Breast Cancer

Drug Information available for: Denosumab

Genetic and Rare Diseases Information Center resources: Inflammatory Breast Cancer

U.S. FDA Resources

Further study details as provided by German Breast Group:

Primary Outcome Measures:

- pcR rates of neoadjuvant treatment with or without denosumab in addition to nab-paclitaxel and EC. [Time Frame: 24 weeks]
- pcR (ypT0 ypN0) rates of nab-Paclitaxel weekly for 12 weeks or 2 of 3 weeks for 12 weeks [Time Frame: 12 weeks]

Secondary Outcome Measures:

- To test for interaction of denosumab treatment with RANK expression. [Time Frame: 24 weeks]
- To assess the pCR rates per arm for both randomizations separately for TNBC and HR-/HER2+ tumors. [Time Frame: 24 weeks]

Estimated Enrollment:	778
Actual Study Start Date:	February 13, 2017
Estimated Study Completion Date:	December 2018
Estimated Primary Completion Date:	December 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Denosumab Denosumab every 4 weeks for 6 cycles.	Drug: Denosumab Denosumab 120 mg every 4 weeks for 6 cycles Other Name: Human monoclonal IgG2 antibody
Experimental: nab-Paclitaxel weekly nab-Paclitaxel weekly for 12 weeks. Patients with HER2-positive tumors receive Trastuzumab and Pertuzumab. Patients with triple-negative tumors receive Carboplatin in parallel to nab-paclitaxel.	Drug: nab-Paclitaxel nab-paclitaxel 125 mg/m² weekly for 12 weeks or at day 1,8 q22 for 4 cycles (12 weeks) Other Name: Abraxane Drug: Carboplatin Carboplatin AUC 2 weekly in parallel to nab-Paclitaxel Other Name: Diamminplatin(II) -cyclobutan-1,1-dicarboxylat Drug: Trastuzumab Trastuzumab 6 (8) mg/kg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Herceptin Drug: Pertuzumab Pertuzumab 420 (840) mg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Perjeta
Experimental: nab-paclitaxel 2 of 3 weeks nab-Paclitaxel day 1,8 q22 for 12 weeks. Patients with HER2-positive tumors receive Trastuzumab and Pertuzumab. Patients with triple-negative tumors receive Carboplatin weekly in parallel to nab-paclitaxel.	Drug: nab-Paclitaxel nab-paclitaxel 125 mg/m² weekly for 12 weeks or at day 1,8 q22 for 4 cycles (12 weeks) Other Name: Abraxane Drug: Carboplatin Carboplatin AUC 2 weekly in parallel to nab-Paclitaxel Other Name: Diamminplatin(II) -cyclobutan-1,1-dicarboxylat Drug: Trastuzumab

	Trastuzumab 6 (8) mg/kg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Herceptin Drug: Pertuzumab Pertuzumab 420 (840) mg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Perjeta
Experimental: EC every two weeks or every three weeks Epirubicin and Cyclophosphamide 600mg/m² for 4 times. Patients with HER2-positive tumors receive Trastuzumab and Pertuzumab.	Drug: Epirubicin Epirubicin 90 mg/m² every 2 or 3 weeks for 4 times Other Name: Farmorubicin Drug: Cyclophosphamide Cyclophosphamide 600 mg/m² every 2 or 3 weeks for 4 times Other Name: Endoxan Drug: Trastuzumab Trastuzumab 6 (8) mg/kg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Herceptin Drug: Pertuzumab Pertuzumab 420 (840) mg every 3 weeks simultaneously to all chemotherapy cycles Other Name: Perjeta

Detailed Description:

RANK ligand (RANKL), a key factor for bone remodeling and metastasis, is crucial for the development of mouse mammary glands during pregnancy. RANKL functions as a major paracrine effector of the mitogenic action of progesterone in mouse and human mammary epithelium via its receptor RANK and has a role in ovarian hormone-dependent expansion and regenerative potential of mammary stem cells. Pharmacologic inhibition of RANKL attenuates the development of mammary carcinoma and inhibits metastatic progression in multiple mouse models.

In a retrospective analysis of 601 patients treated in the GeparTrio study with chemotherapy (TAC) it could be demonstrated that elevated expression of RANK (immunohistochemical score > 8.5 using the N-1H8 antibody by Amgen) was found in 14.5% of patients overall, with a significant predominance in patients with hormone-receptor-negative disease (33.7% vs 6.4% tumors positive for RANK). Expression of RANK was associated with a higher pathological complete response rate (pCR) (23.0% vs 12.6%) but with a shorter disease-free and overall survival. The ABCSG-18 study showed that adjuvant denosumab reduces clinical fractures, improves bone health, and can be administered without added toxicity. Moreover denosumab improves disease-free survival in postmenopausal woman with hormone receptor positive breast cancer.

It appears therefore reasonable to test denosumab, a clinically available antibody against RANKL in patients with hormone-receptor-negative primary breast cancer as an adjunct to neoadjuvant chemotherapy for its ability to increase pCR rate and improve outcome in relation to the expression of RANK.

Eligibility

Ages Eligible for Study:	18 Years to 75 Years (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion criteria:

- Unilateral or bilateral primary carcinoma of the breast, confirmed histologically by core biopsy. Fine-needle aspiration from the breast lesion alone is not sufficient. Incisional biopsy or axillary clearance is not allowed. In case of bilateral cancer, the investigator has to decide prospectively which side will be evaluated for the primary endpoint.
- Tumor lesion in the breast with a palpable size of 2 cm or a sonographical size of 1 cm in maximum diameter. The lesion has to be measurable in two dimensions, preferably by sonography. In case tumor isn't measurable by sonography, then MRI or mammography is sufficient. In case of inflammatory disease, the extent of inflammation can be used as measurable lesion.
- Patients must have stage cT1c - cT4a-d disease.
- In patients with multifocal or multicentric breast cancer, the largest lesion should be measured.
- Centrally confirmed ER-negative and PR-negative status. Central pathology includes also assessment of HER2, Ki-67, TIL and RANK status on core biopsy. ER/PR negative is defined as ≤1% stained cells and HER2-positive is defined as IHC 3+ or in-situ hybridization (ISH) and according to ASCO-CAP guidelines as of 2013. LPBC (lymphocyte predominant breast cancer) is defined as more than 50% stromal tumour infiltrating lymphocytes. Formalin-fixed, paraffin-embedded (FFPE) breast tissue from core biopsy has therefore to be sent to the GBG central pathology laboratory prior to randomization.

Exclusion criteria:

- Patients with stages cT1a, cT1b, or any M1.
- Prior chemotherapy for any malignancy.
- Prior radiation therapy for breast cancer.
- History of disease with influence on bone metabolism, such as osteoporosis, Paget's disease of bone, primary hyperparathyroidism requiring treatment at the time of randomization or considered likely to become necessary within the subsequent six months.
- Use of bisphosphonates or denosumab within the past 1 year.
- Significant dental/oral disease, including prior history or current evidence of osteonecrosis/ osteomyelitis of the jaw, active dental or jaw condition which requires oral surgery, non-healed dental/oral surgery, planned invasive dental procedure for the course of the study.
- Previous malignant disease 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.
- Currently active infection.
- Incomplete wound healing.
- Definite contraindications for the use of corticosteroids.

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: NCT02682693

Contacts

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Locations

Germany

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Sponsors and Collaborators

German Breast Group

Amgen

Celgene Corporation

Investigators

Principal Investigator: Sherko Kümmel, MD Kliniken Essen-Mitte

More Information

Responsible Party:	German Breast Group
ClinicalTrials.gov Identifier:	NCT02682693 History of Changes
Other Study ID Numbers:	GBG 88
Study First Received:	January 27, 2016
Last Updated:	July 10, 2017

Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No

Additional relevant MeSH terms:

Breast Neoplasms	Albumin-Bound Paclitaxel
Inflammatory Breast Neoplasms	Cyclophosphamide
Carcinoma, Ductal, Breast	Carboplatin
Neoplasms by Site	Trastuzumab
Neoplasms	Epirubicin
Breast Diseases	Denosumab
Skin Diseases	Antineoplastic Agents, Phytogenic
Carcinoma, Ductal	Antineoplastic Agents
Adenocarcinoma	Tubulin Modulators
Carcinoma	Antimitotic Agents
Neoplasms, Glandular and Epithelial	Mitosis Modulators
Neoplasms by Histologic Type	Molecular Mechanisms of Pharmacological Action
Neoplasms, Ductal, Lobular, and Medullary	Immunosuppressive Agents
Paclitaxel	Immunologic Factors
Pertuzumab	Physiological Effects of Drugs

ClinicalTrials.gov processed this record on August 04, 2017