KURZPROTOKOLL
GAIN II

Öffentlicher Titel	Phase III Studie zu nab-Paclitaxel bei Hochrisiko Brustkrebs in einem frühen Stadium
Wissenschaftl. Titel	Adjuvant Phase III Trial to Compare Intense Dose-dense Adjuvant Treatment With EnPC to Dose Dense, Tailored Therapy With dtEC-dtD for Patients With High-risk Early Breast Cancer
Kurztitel	GAIN II
Studienart	multizentrisch, prospektiv, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase III
Erkrankung	Geschlechtsorgane: Brustkrebs: adjuvant
Einschlusskriterien	- Written informed consent for all study procedures according to local regulatory requirements prior to beginning specific protocol procedures - Histologically confirmed unilateral or bilateral primary carcinoma of the breast - Age at diagnosis at least 18 years, female, and biologically not older than 65 years - Adequate surgical treatment with histological complete resection (R0) of the invasive breast tumor. Choice of axilla surgery (clearance or sentinel node biopsy) is up to the participating site. - Centrally confirmed ER/PR/HER2 and Ki-67 status detected on surgical biopsy. ER/PR positive is defined as >=1% stained cells and HER2-positive is defined as IHC 3+ in >10% immunoreactive cells or FISH (or equivalent test) ratio 2.0. Formalin-fixed, paraffin-embedded (FFPE) breast tissue has therefore to be sent to the Dept. of Pathology at the Charité, Berlin prior to randomization - High risk breast cancer as defined as: a) HER2-positive or triple-negative tumors irrespective of nodal status; b) luminal B-like tumors (ER and/or PgR positive, HER2 negative, Ki-67 >20%) with involved lymph nodes; c) 4 or more involved lymph nodes - Complete staging work-up within 3 months prior to randomization. All patients must have bilateral mammography, breast ultrasound, breast MRI (optional), chest X-ray (PA and lateral), abdominal ultrasound or CT scan or MRI and bone scan done. In case of positive bone scan, bone X-ray (or CT or MRI) is mandatory. Other tests may be performed as clinically indicated - Karnofsky Performance status index at least 80% - Estimated life expectancy of at least 10 years irrespective of the diagnosis of breast cancer - Confirmed normal cardiac function by ECG and cardiac ultrasound (LVEF or shortening fraction) within 2 weeks prior to randomization for patients with HER2-positive disease. LVEF must be above 55% - Laboratory requirements: a) Haematology; b) Absolute neutrophil count (ANC) at least 2.0 x 10^9/L and Platelets at least 100 x 10^9/L and; c) Hemoglobin at least 10 g/dL (6.2 mmol/L) Hepatic function; d) Total bilirubin <= 1.5x times above upper normal limits (UNL) and; e) ASAT (SGOT) and ALAT (SGPT) more tham 1.5x UNL and; f) Alkaline phosphatase more than 2.5x UNL. Renal function; g) Creatinine <= 1.25 UNL; h) Creatinine Clearance > 30ml/min (if Creatinine is above UNL, according to Cockcroft-Gault) - Negative pregnancy test (urine or serum) within 14 days prior to randomization for all women of childbearing potential - Complete baseline documentation must be submitted via MedCODES® and approved by GBG Forschungs GmbH - Patients must be available and compliant for central diagnostics, treatment and follow-up.
Ausschlusskriterien	- Patients with luminal A-like tumors (ER and or PgR positive, HER2 negative and Ki-67 <= 20%)and less than 4 involved lymph nodes

- Non-operable breast cancer
- Time since axillary dissection or SLNB >3 months (optimal < 1 month)
- Previous and already (neoadjuvant or adjuvant) treated invasive breast carcinoma
- 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 >160 / 90 mm Hg under treatment with two antihypertensive drugs), rhythm abnormalities requiring permanent treatment, clinically significant valvular heart disease
- Evidence for infection including wound infections, HIV, hepatitis
- History of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent
- Pre-existing motor or sensory neuropathy of a severity at least grade 1 by NCI-CTC criteria v 4.0
- Other severe and relevant co-morbidity that would interact with the application of cytotoxic agents or the participation in the study
- Previous or concurrent treatment with: a) concurrent chronic corticosteroids unless initiated > 6 months prior to study entry and at low dose (less than 10 mg methylprednisolone or equivalent) (except inhalative corticoids); b) concurrent sex hormones. Prior treatment must be stopped before study entry; c) concurrent treatment with any investigational, not marketed drug within 30 days prior to study entry; d) previous or concurrent anti-cancer therapy for any reason
- Absolute contraindications for the use of corticosteroids
- Pregnant or lactating patients. Patients of childbearing potential must implement adequate non-hormonal contraceptive measures (barrier methods, intrauterine contraceptive devices, sterilization) during study treatment
- Known hypersensitivity reaction to one of the compounds or incorporated substances used in this protocol.

Alter	18 Jahre und älter
Molekularer Marker	Triple neg (HER2/ER/PR neg)
	HER2/neu neg./ER pos.
	HER2/neu neg./PR pos.
	HER2/neu pos.
Sponsor	German Breast Group (Hauptsponsor)
Förderer	Celgene GmbH
	AMGEN GmbH
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT01690702 EudraCT 2011-005214-11