KURZPROTOKOLL
ADAPT

Öffentlicher Titel	Optimierungsstudie zu Risikoanalyse und Prognose des Behandlungserfolgs mittels Biomarkern bei Brustkrebs im Frühstadium
Wissenschaftl. Titel	Adjuvant Dynamic marker-Adjusted Personalized Therapy trial optimizing risk assessment and therapy response prediction in early breast cancer
Kurztitel	ADAPT
Studienart	Therapiestudie, randomisiert, offen/unverblindet, kontrolliert, mehrarmig
Studienphase	nicht zutreffend
Erkrankung	Geschlechtsorgane: Brustkrebs: adjuvant
Ziele	- The ADAPT trial aims at personalizing therapy in early breast cancer by integration of dynamic response data into clinical management and at sparing unnecessary therapies without compromising patient outcome. - Identification of a responder sub-population with intermediate and high risk, which due to therapy has outcome comparable to HR+/RS 11 - Disease-free and overall survival in corresponding groups - Overall survival - Toxicity - Cost-effectiveness - distant disease-free survival (DDFS) - local and regional relapse-free survival (LRFS and RRFS)
Einschlusskriterien	- Female patients, age at diagnosis 18 years and above (consider ADAPT Elderly for patients at 70 years and above) - Histologically confirmed unilateral primary invasive carcinoma of the breast - T1 - T4 (except inflammatory breast cancer) - All N - Patients should be candidates for adjuvant chemotherapy according to conventional prognostic factors - No clinical evidence for distant metastasis (M0) - Known HR status and HER2 status (local pathology) - Tumor block available for central pathology review - Performance Status ECOG <= 1 or KI >= 80% - Negative pregnancy test (urine or serum) within 7 days prior to registration in premenopausal patients - Written informed consent prior to beginning specific protocol procedures, including expected cooperation of the patients for the treatment and follow-up, must be obtained and documented according to the local regulatory requirements - The patient must be accessible for treatment and follow-up - Additional Inclusion criteria for patients receiving chemotherapy: - Laboratory requirements for patients receiving chemotherapy (within 14 days prior to randomization): o Leucocytes >= 3.5 10^9/L o Platelets >= 100 10^9/L o Hemoglobin >= 10 g/dL o Total bilirubin <= 1 x ULN o ASAT (SGOT) and ALAT (SGPT) <= 2.5 UNL o Creatinine <= 175 µmol/L (2 mg/dl) - LVEF within normal limits of each institution measured by echocardiography and normal ECG (within 42 days prior to randomization) - Additional Inclusion Criteria ADAPT HR+/HER2- Breast Cancer In order to be eligible for the participation in the ADAPT HR+/HER2- breast cancer trial, patients who meet the general inclusion/exclusion criteria of the ADAPT trial also have to meet the following additional inclusion criteria:

- ER and/or PR positive and HER2 negative
- Central pathology available (Grading, Ki-67, RS)
- All patients should be recommended to be treated by adjuvant chemotherapy in the daily routine practice by one of the current guildeines (St. Gallen, AGO Mamma, S3, ESMO) or to be high clinical risk by AdjuvantOnline (breast cancer specific survival of <88%) - Clinically N+ or cN0 with one of following features: G3, <35 years old, KI-67>14%; if G2 cT>1, If G1 only if clinical tumor size >3 cm - If Clinical decision is based on AdjuvantOnline patients should derive more than 5% 10-year relapse-free survival benefit by use of chemotherapy (3rd generation anthracycline/taxane-based) additional to standard endocrine therapy (using clinical T and N status)
- Additional Inclusion Criteria ADAPT HR+/HER2- Part II To be eligible for the participation in the ADAPT HR+/HER2- trial part II (neo)adjuvant chemotherapy question) the patients have to meet all of the additional inclusion criteria mentioned above plus one of the following inclusion criteria:
- More than 3 involved lymph nodes (c/pN2-3) • N0-1 and RS 26 • N0-1 and RS 12-25 with Ki-67post > 10% • G3 with Ki-67 40% in tumors >1cm
- Patients with tumors cT2 and/or cN+ are strongly recommended to be treated by neoadjuvant chemotherapy

Ausschlusskriterien

- Known hypersensitivity reaction to the compounds or incorporated substances
- Prior malignancy with a disease-free survival of < 10 years, except curatively treated basalioma of the skin, pTis of the cervix uteri
- Non-operable breast cancer including inflammatory breast cancer
- Previous or concurrent treatment with cytotoxic agents for any reason after consultation with the sponsor
- Concurrent treatment with other experimental drugs. Participation in another interventional clinical trial with or without any any investigational not marketed drug within 30 days prior to study entry
- Male breast cancer
- Concurrent pregnancy; patients of childbearing potential must implement a highly effective (less than 1% failure rate) non-hormonal contraceptive measures during the study treatment
- Breast feeding woman
- Sequential breast cancer
- Reasons indicating risk of poor compliance
- Patients not able to consent
- Additional Exclusion Criteria for patients receiving chemotherapy:
- Known polyneuropathy grade 2
- Severe and relevant co-morbidity that would interact with the application of cytotoxic agents or the participation in the study
- Uncompensated cardiac function
- Inadequate organ function including: o Leucocytes <= 3.5 x 10^9/l o Platelets <= 100 x 10^9/l o Bilirubin above normal limits o Alkaline phosphatase >= 5 x UNL o ASAT and/or ALAT associated with AP > 2.5 UNL
- Additional Exclusion Criteria ADAPT HR+/HER2-: Patients with clinical low risk tumors, who are not treated by adjuvant chemotherapy in the daily practice (e.g. cT1, G1, cN0)
- Additional Exclusion Criteria ADAPT HR+/HER2- Part II:
- Known polyneuropathy grade 2

	- Severe and relevant co-morbidity that would interact with the application of cytotoxic agents or the participation in the study - Uncompensated cardiac function - Inadequate organ function including: o Leucocytes < 3.5 x 109/l o Neutrophils <1.5 x 109/l o Platelets < 100 x 109/l o Bilirubin above normal limits o Alkaline phosphatase >= 5 x UNL o ASAT and/or ALAT > 2.5 x UNL
Alter	18 Jahre und älter
Molekularer Marker	HER2/neu neg./ER pos. HER2/neu neg./PR pos.
Fallzahl	5236
Sponsor	West German Study Group
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT01779206 EudraCT 2011-001462-17