KURZPROTOKOLL
Detect-III

Öffentlicher Titel	Phase III Studie bei initial HER2-neg Brustkrebs und HER2-pos zirkulierenden Tumorzellen
Wissenschaftl. Titel	A multicenter, randomized, phase III study to compare standard therapy alone versus standard therapy plus Lapatinib in patients with initially HER2-negative metastatic breast cancer and HER2-positive circulating tumor cells
Kurztitel	Detect-III
Studienart	multizentrisch, randomisiert, offen/unverblindet, zweiarmig
Studienphase	Phase III
Erkrankung	Geschlechtsorgane: Brustkrebs: Zweitlinie oder höher
Ziele	- The primary objective of the trial is to prove the clinical efficacy of lapatinib (as assessed by the CTC clearance rate) in patients with metastasizing breast cancer who exhibit HER2-positive circulating tumor cells (CTC) although the primary tumor tissue and/or biopsies from metastatic sites were investigated for HER2 status and showed HER2-negativity.
Einschlusskriterien	- Written informed consent in study participation. - Metastatic breast cancer which cannot be treated by surgery or radiotherapy only. The primary tumor and/or biopsies from metastatic sites or locoregional recurrences must have been con-firmed as cancer by histopathology. Estrogen Receptor (ER) and Progesterone Receptor (PgR) status must have been documented. - All primary tumor tissue and/or biopsies from metastatic sites or locoregional recurrences that were investigated for HER2 status showed HER2-negativity (i.e.: immunohistochemistry (IHC) score 0-1+ or 2+ and fluorescent in situ hybridization (FISH) negative or just FISH neg-ative, whichever was performed). In patients for which standard HER2-testing was not available at time of primary diagnosis and for which a biopsy of metastatic sites or locoregional recurrences were not performed are regarded as having a HER-2 negative tumor. - Evidence of HER2-positive CTCs. Evidence is assumed if the following holds: • At least one CTC could be extracted from 7.5 ml patient blood by means of the Cell-Search® Circulating Tumor Cell Kit (Veridex LLC, Raritan, USA) and • At least one of all extracted CTCs was found to be HER2-positive. HER2 status must be assessed by means of IHC or FISH. - Indication for a standard chemo- or endocrine therapy whose combination with lapatinib is either approved (see SPC of Tyverb® 250 mg tablets) or has been investigated in prior clinical trials (see tables of section 8.2.1.). - Tumor evaluation has been performed within 6 weeks before randomization and results are available. - Patients must have at least one lesion that can be evaluated according to RECIST guideline version 1.1. Patients with measurable and/or non-measurable disease are eligible. [Eisenhauer 2009]. - Age 18 years. - ECOG Score < 2. - Adequate organ function within 7 days before randomization, evidenced by the following labo-ratory results below: absolute neutrophil count 1500/µL; platelet count 100000/µL; hemoglobin 9g/dL; ALT (SGPT) 3.0 × ULN; AST (SGOT) 3.0 × ULN; Bilirubin 2 × ULN and 35% direct; creatinine 2.0 mg/dl or 177µmol/L - Left ventricular cardiac ejection fraction (LVEF) 50%, within normal institutional limits as measured by echocardiogram.

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- In case of patients of child bearing potential:Negative pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 7 days prior to randomization, Contraception by means of a reliable method (i.e. non-hormonal contraception, IUD, a double barrier method, vasectomy of the sexual partner, complete sexual abstinence). Pa-tient must consent in maintaining such contraception until 28 days after completion of study treatment.

Ausschlusskriterien

- History of hypersensitivity reactions attributed to compounds of similar chemical or biological composition to lapatinib.
- History of > 3 chemotherapy lines for metastatic disease (a chemotherapy line being defined as any new chemotherapy and any modification of an existing chemotherapy regimen regardless of the reason for change).
- Treatment with investigational agents of any type or anticancer therapy during the trial or with-in 2 weeks prior to randomization and 6 weeks in case of nitrosoureas or mitomycin C.
- Adverse events due to prior anticancer therapy which are > Grade 1 (NCI CTCAE) and therapeutically relevant at time of randomization.
- Anti-retroviral therapy due to HIV infection.
- Current active hepatic or biliary disease (with exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator as-sessment)
- Concurrent disease or condition that might interfere with adequate assessment or evaluation of study data, or any medical disorder that would make the patient's participation unreasonably hazardous.
- Other malignant diseases within the last 3 years apart from CIN of the uterine cervix and skin basalioma.
- Disease or condition which might restrain the ability to take or resorb oral medication. This includes malabsorption syndrome, requirement for intravenous (IV) alimentation, prior surgi-cal procedures affecting absorption (for example resection of small bowel or stomach), uncon-trolled inflammatory GI disease (e.g., Crohn's disease, ulcerative colitis) and any other dis-eases significantly affecting gastrointestinal function as well as inability to swallow and retain oral medication for any other reason.
- Active cardiac disease, defined as:History of uncontrolled; history of arrhythmias requiring medications, or clinically significant, with the exception of asymptomatic atrial fibrillation requiring anticoagulation; myocardial infarction less than 6 months from study entry; uncontrolled or symptomatic congestive heart failure; ejection fraction below the institutional normal limit; any other cardiac condition, which in the opinion of the treating physician would make this protocol unreasonably hazardous for the patient.
- Dementia, altered mental status, or any psychiatric or social condition which would prohibit the understanding or rendering of informed consent or which might interfere with the patient's adherence to the protocol.
- Life expectancy < 3 months.
- Male patients.
- Pregnancy or nursing.
- Primary tumor or biopsies from metastatic sites or locoregional recurrences showing HER2-positivity.
- Any prior treatment with anti-HER2 directed therapy

Alter

18 Jahre und älter

Molekularer Marker

HER2/neu neg.

HER2/neu pos.

Fallzahl

120

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Prüfzentren	**Main-Kinzig-Kliniken** (Rekrutierung beendet) Herzbachweg 14 63571 Gelnhausen Gudrun Riegel Tel: 06051 872448 Fax: 06051 872035 gudrun.riegel@mkkliniken.de
	Klinikum Frankfurt Höchst (Rekrutierung beendet) Klinik für Gynäkologie und Geburtshilfe Gotenstraße 6-8 65929 Frankfurt am Main Prof. Dr. Joachim Rom joachim.rom@varisano.de
	Klinikum Hanau GmbH (Rekrutierung beendet) Klinik für Gynäkologie und Geburtshilfe Leimenstraße 20 63450 Hanau PD. Dr. med. Thomas Müller Tel: 06181 296-2500 Fax: 06181 296-2540 klinikgyngeb@klinikum-hanau.de
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