DETECT III - A multicenter, randomized, phase III trial 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


- on behalf of the DETECT study group

Background

HER2 status may change over the course of disease in breast cancer pts. Approx. 20-30% of pts with initially HER2-negative breast cancer have HER2-positive metastasis (Zidan et al. 2005; Tewes et al. 2009). Determining HER2 status on CTC is one option to re-evaluate HER2 status and to use CTCs as a liquid biopsy at the time metastasis is diagnosed. Currently it is unclear if HER2-targeted therapy based on the assessment of HER2 status of CTC reveals a clinical benefit. Therefore, the study DETECT III aims to assess whether lapatinib, as one of the HER2-targeted therapies, in initially HER2-negative breast cancer patients with HER2-positive CTC is effective at the time of distant disease.

Trial Design

Main Eligibility Criteria

- Metastatic breast cancer
- HER2-negative primary tumor tissue and/or biopsies from metastatic sites or locoregional recurrences
- Evidence of HER2-positive CTCs
- Indication for a standard chemo- or endocrine therapy whose combination with lapatinib is either approved or has been investigated in prior clinical trials (see Table 1)
- ≥1 lesion, according to RECIST 1.1

Lapatinib + Monotherapies Recommended Treatment Regimen

<table>
<thead>
<tr>
<th>Lapatinib + doxorubicin</th>
<th>Recommended Treatment Regimen</th>
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<tbody>
<tr>
<td>Daily lapatinib (1125 mg) + docetaxel (75 mg/m² q3w.) after discontinuation of initial lapatinib mono 1125 mg daily.</td>
<td></td>
</tr>
</tbody>
</table>

Lapatinib + paclitaxel

Daily lapatinib (1125 mg) + paclitaxel (80 mg/m² weekly), or daily lapatinib (1125 mg) and paclitaxel (175 mg/m² q3w.) after discontinuation of paclitaxel mono 175 mg/m² daily.

Lapatinib + capecitabine

Daily lapatinib (1125 mg) + capecitabine (825 mg/m² q3w.) after discontinuation of capecitabine mono 825 mg/m² daily.

Lapatinib + vinorelbine

Daily lapatinib (1125 mg) + vinorelbine (25 mg/m² q3w.), 8 pts.

Lapatinib + NPLD (non-plated liquid pathological dissection)

Daily lapatinib (1125 mg) + NPLD (~1000 μl/m² q3w.), 8 pts.

Table 1: Treatment Options within DETECT III

Specific Aims

The objective of the trial is to prove the clinical efficacy of lapatinib in patients with metastatic breast cancer who exhibit HER2-positive circulating tumor cells (CTC) although the primary tumor tissue and/or biopsies from metastatic sites showed HER2-negativity. Primary endpoint is progression free survival. Secondary endpoints include overall response rate, clinical benefit rate, overall survival and dynamic of CTC.

CCT - Determination

To determine CTCs and HER2-status the CellSearch®-System (Veridex, USA) is used. After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labeled with anti-CXK/18/19, anti-CD45 antibodies as well as a fluorescein conjugate antibody for HER2-phenotyping. To be eligible pts must have ≥1 CTC with strong HER2-staining (+++).

Figure 2: Screenshots of CTC-Determination

Recruitment

The DETECT III trial started recruiting in February 2012. The number of participating sites in Germany and enrolled patients are shown in table 2, updated 23rd November 2012.

Table 2: Number of Participating Sites and Enrolled Patients

<table>
<thead>
<tr>
<th>Study-sites</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>108</td>
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<tr>
<td>Open</td>
<td>90</td>
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<tr>
<td>Active</td>
<td>52</td>
</tr>
</tbody>
</table>

References


Acknowledgment

