

# DETECT III/IV - two combined clinical trials based on the phenotype of circulating tumor cells (CTCs)

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## Background

Although the prognostic value of CTC enumeration in metastatic breast cancer (MBC) is well established, the potential of molecular characterization of CTCs for improvement of treatment decisions requires further investigation.

## Trial Design

The DETECT studies are prospective, multicenter, open-label clinical trials designed for patients with HER2-negative MBC and CTCs in the peripheral blood.

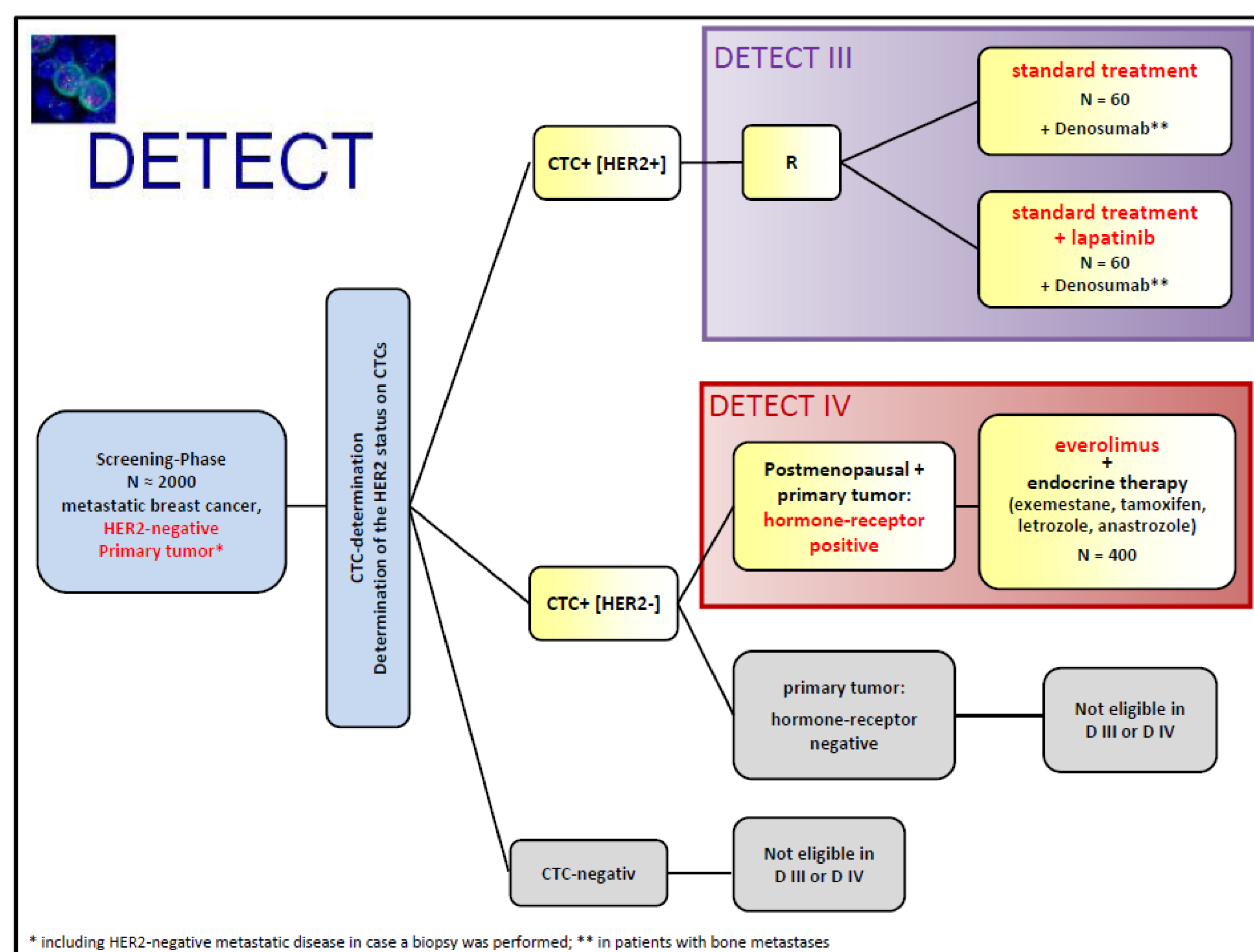


Figure 1: Trial Design DETECT III / IV

## Main Eligibility Criteria

- Metastatic breast cancer
- HER2-negative primary tumor tissue and / or HER2-negative biopsies from metastatic sites
- Evidence of at least one CTC in 7,5 mL blood
- ≥ 1 lesion evaluable according to RESIST

## Specific Aims

The primary objective of both trials is to estimate the clinical efficacy of treatments, assessed by the CTC clearance rate for DETECT III and progression-free survival (PFS) for DETECT IV.

## Methods

Prevalence of CTCs at various time points as well as the HER2 status of CTCs will be determined using the FDA-approved CellSearch System (Veridex, USA). Survival endpoints will be estimated using the Kaplan-Meier method.

## Present and Target Accrual

Overall, about 2000 MBC patients with a HER2-negative primary tumor will be screened in order to randomize 120 patients with HER2-positive CTCs for DETECT III (which started in February 2012) and 400 patients with HER2-negative CTCs for DETECT IV (which started in December 2013). So far, over 800 patients were screened and tested for CTCs.

## Perspectives

The DETECT III trial is the first study with treatment based on phenotypic characteristics of CTCs. If this trial succeeds in proving efficacy of lapatinib in patients with HER2-negative primary tumor but HER2-positive CTCs, it may lead to new treatment strategies for MBC. DETECT IV complements DETECT III with additional therapy options in patients with HER2-negative CTCs. The study concept of these clinical trials with therapy decisions based on prevalence and molecular phenotype of CTCs could be an important step towards a more personalized cancer treatment for MBC.

In addition, the DETECT IV trial is planned to be amended by a second treatment cohort with eribulin for patients with triple negative MBC or HER2-negative and hormone-receptor positive MBC and indication for chemotherapy. Thus, the DETECT studies offer innovative therapy intervention for the majority of patients with detectable CTCs in MBC.