

Figure 2. Study design of STIC circulating tumor cells (CTCs) initiated by the Institut Curie in Paris^[26]

if chemotherapy was administered ($P = 0.001$ for PFS and $P = 0.04$ for OS). Thus, it could be shown for the first time that CTC-based therapy intervention led to better clinical outcome. However, it is difficult to translate these results into the clinical routine, since new substances, most importantly the CDK4/6 inhibitors, have been approved for treatment of HR-positive HER2-negative MBC after the initiation of the STIC CTC trial and nowadays more than 60% of this subgroup receive endocrine-based combination therapy in the first-line setting^[27].

Other currently recruiting trials focus on the characteristics of CTCs rather than their numbers. Most notably, the German DETECT study program aims at establishing a possible benefit of targeted therapies chosen according to the receptor status of CTCs and not primary tumor or metastasis [Figure 3]. Previous data have shown that CTCs frequently differ from cells in the primary tumor or metastasis with regard to prognostic and predictive markers^[28-30]. In the phase III DETECT III trial, patients with HER-negative MBC are screened for HER2-positive CTCs and, if such cells are detected, they are randomized to standard therapy \pm anti-HER2 therapy lapatinib. Patients with HER2-negative CTCs are available for DETECT IVa and IVb trials and those with HER2-positive MBC can participate in the phase III DETECT V study.

CONCLUSION

In the last decades, blood-based diagnostics have become one of the major focuses of oncological and translational research. Elevated levels of CTCs and tumor DNA serve as an important prognostic factor in metastatic BC and can complement therapy monitoring. Beyond enumeration, assessment of mutational status of ctDNA and phenotypic features of CTCs holds great promise in terms of liquid biopsy-guided treatment interventions. In 2019, the SOLAR-1 trial led to the first liquid biopsy-based approval in MBC in the history of the FDA. Furthermore, the French STIC CTC trial has become the first study on liquid biopsy-based interventions to demonstrate that enumeration of CTCs may guide treatment decisions in metastatic BC.

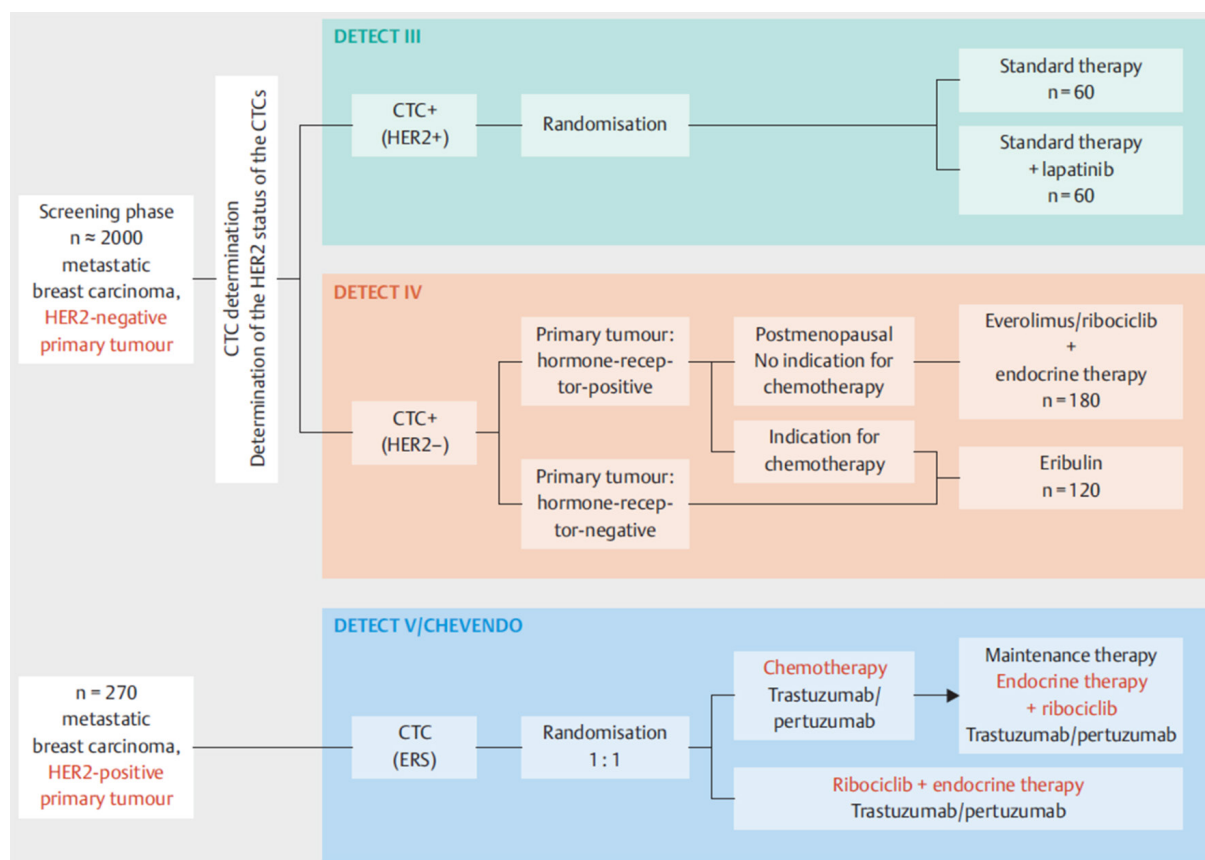


Figure 3. Design of the studies within the DETECT trial program - the largest study program on circulating tumor cell (CTC)-guided therapies worldwide^[11]

DECLARATIONS

Authors' contributions

Manuscript writing and editing: Banys-Paluchowski M, Paluchowski P

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

Banys-Paluchowski M received lecture honoraria and served in advisory role for Roche, Novartis, Pfizer, and Eli Lilly. Paluchowski P declares no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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