INTRODUCTION

HER2-positive advanced breast cancer (ABC) is associated with an aggressive tumor behavior, poor response rates to chemotherapy, high relapse rates and high incidences of brain metastases (BM). Tucatinib, a novel highly selective HER2 tyrosine kinase inhibitor, in combination with trastuzumab and capecitabine has demonstrated a significant overall and progression-free survival benefit compared to placebo + trastuzumab + capecitabine in patients pretreated with trastuzumab, pertuzumab and trastuzumab-emtansine in the pivotal HER2CLIMB trial. For patients with BMs, intracranial response rates were higher with the tucatinib combination compared to the placebo combination. Moreover, the risk of developing new BM or death was reduced by 48% in all patients with or without brain metastases in the tucatinib combination. The tucatinib combination has recently been approved in European Union for HER2-positive ABC patients with at least two prior anti-HER2 treatment regimens (in any setting). However, real-world data without strict in- and exclusion criteria are still limited. Additionally, data on tucatinib in early treatment lines (1st and 2nd line) are scarce.

METHODS

The prospective non-interventional study TRACE (NCT0253911) will enroll 300 patients with HER2-positive ABC scheduled to receive tucatinib + trastuzumab + capecitabine according to summary of product characteristics (SmPC). Patients each will be enrolled into the 1st and 2nd line and the 3rd and 4th line cohort (Figure 3). Patients will be enrolled within 36 months at 60 sites across Germany (start of enrollment in May 2022). Key in- and exclusion criteria are listed in Figure 2.

Primary endpoints is time to deterioration and change from baseline in all scores of the EQ-5D-5L, EORTC QLQ-C30 and QLQ-BR23 questionnaires. Secondary endpoints are on health-related quality of life (HRQoL) will be assessed by validated questionnaires EQ-5D-5L, EORTC QLQ-C30 and QLQ-BR23. HRQoL will be assessed at baseline before start of treatment, every 2 months during tucatinib + trastuzumab + capecitabine treatment and every 3 months thereafter for a maximum of 24 months. Treatment reality of enrolled patients will be intensively documented during tucatinib + trastuzumab + capecitabine treatment and will be followed up regarding subsequent therapies, progression and survival. Documentation of all patients will end at the latest 24 months after finalization of enrollment (i.e., last patient in, LPI) (Figure 3).

Study design
TUCATINIB IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC HER2-POSITIVE BREAST CANCER WHO RECEIVED AT LEAST TWO PRIOR ANTI-HER2 TREATMENT REGIMENS

CONCLUSION

Over the next 5 years, TRACE will provide valuable real-world data not only on treatment with tucatinib + trastuzumab + capecitabine in the 1st to 4th line setting, but also on treatment reality and the changing treatment landscape of patients with HER2-positive ABC. TRACE will focus on HRQoL. Effectiveness and safety in real-world will also be assessed and preplanned subgroup analyses will fill important knowledge gaps.

Key inclusion criteria
- Aged 18 years or older.
- Diagnosis of locally advanced or metastatic HER2-positive breast cancer, including patients with brain metastases.
- Prior therapy with at least two prior anti-HER2 treatment regimens.
- Decision for treatment with tucatinib in combination with trastuzumab and capecitabine according to current summary of product characteristics (SmPC) either in 1st 2nd palliative treatment line (cohort 1) or 3rd 4th palliative treatment line (cohort 2).
- Patients in cohort 2 must have been diagnosed with locally advanced and unresectable or metastatic disease at primary diagnosis.
- Progression or intolerance to last systemic anti-HER2-based therapy.
- Indication for treatment with tucatinib as assessed by the treating physician.
- Signed written informed consent.

Key exclusion criteria
- Contraindications according to current SmPC of tucatinib.
- Administration of study treatment in 5th or higher palliative therapy line.
- Onset of tucatinib treatment later than 2 days after start of therapy line.

Figure 1: Expected time schedule

Figure 2: Key in- and exclusion criteria

Figure 3: Key inclusion criteria

For a complete list of criteria please see (https://clinicaltrials.gov/ct2/show/NCT0253911)