Can resistance to trastuzumab be reversed by endocrine therapy? Combination of trastuzumab and letrozole after resistance to sequential trastuzumab and aromatase inhibitor monotherapies in patients with ER-positive, HER-2 positive, advanced breast cancer: a proof-of-concept trial (SAKK 23/03)

On behalf of the Swiss Group for Clinical Cancer Research (SAKK)

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Abstract (updated)

Background & Hypothesis

We hypothesized that the clinical relevance of the upfront combined inhibition of hormonal and growth factor pathways was undefined, and a sequential approach might be advantageous. Thus a sequential treatment design was chosen in this proof-of-concept trial to ensure complete clinical resistance to single agent treatments before receiving both a non-steroidal aromatase inhibitor (AI) and trastuzumab (T) given as monotherapy before receiving both agents in step 2.

Key eligibility criteria

- Histopathologically or cytologically confirmed diagnosis of breast cancer
- ER+ and/or PgR+ ≥ 10% (immunohistochemistry)
- HER-2+ (assessed by FISH, ratio ≥ 2)

Results

Thirteen patients were enrolled. In step 1, six patients (46%) achieved clinical benefit rate (CBR: CR, PR or DS ≥ 6 months) in step 2. Progression-free survival (PFS) was 12.6 months (95% CI: 3.8-NC). CBR was observed in eight out of the eleven evaluable patients (73%) in step 2, including one patient with partial response. Median PFS for all patients was 188 days (95% CI: 77-NC). In step 1, treatment-related toxicities were generally manageable.

Conclusion: Results of this proof-of-concept trial suggest that complete resistance to both AI and T can be overcome in a proportion of patients by combined treatment of AI and T, as all patients served as their own control. Our results appear promising for a new treatment strategy which offers a chemotherapy-free option for at least a subset of patients with ER+ breast cancer.

References:


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