TARGETED THERAPIES

Chemotherapy-free option for relapsed patients with breast cancer

Although the standard-of-care for most women with HER2-positive breast cancer is trastuzumab combined with chemotherapy, a small number of patients prefer to avoid chemotherapy completely. Dieter Köberle and coworkers initiated a trial to identify if trastuzumab combined with an aromatase inhibitor (AI) would produce clinically meaningful responses. “We speculated that the relationship between the estrogen pathway and the HER2 pathway is dynamic ... we thought that only a sequential trial methodology would be able to give a hint of this interaction,” explains Köberle.

The multicenter, two-step, phase II trial was conducted in 13 patients with advanced-stage breast cancer that was positive for estrogen receptor and *HER2* expression. Participants, with progressive disease on prior treatment with an AI, received trastuzumab until progression in the first step, and then trastuzumab

combined with letrozole in the second step. In step two, in patients who would usually be considered to be refractory to trastuzumab, clinical benefit was observed in eight patients, with one partial response. In all evaluable patients, the median time-to-progression in step two was 188 days.

“These are absolutely new (and as yet unvalidated) clinical data and results were much better than expected, thus supporting this ‘non-chemo’ approach,” notes Köberle. In a small subset of patients this less-toxic treatment approach might be preferable to current standard-of-care.

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Original article Koeberle, D. *et al.* Combination of trastuzumab and letrozole after resistance to sequential trastuzumab and aromatase inhibitor monotherapies in patients with estrogen receptor-positive, HER-2-positive advanced breast cancer: a proof-of-concept trial (SAKK 23/03). *Endocr. Relat. Cancer* **18**, 257–264 (2011)