Treatment of breast cancer with the fetal estrogen estetrol (E4)

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High dose estrogens was the endocrine treatment of choice in postmenopausal women with advanced breast cancer for several decades since 1944. In the 1970s, estrogen therapy was replaced by tamoxifen. Tamoxifen showed similar regression rates but less toxicity as compared to estrogen therapy and was therefore preferred. Recently, estrogen therapy has gained new interest as several clinical studies showed clinical benefit in heavily pre-treated patients with advanced breast cancer in an estrogen deprived setting. Estrogen therapy is an effective treatment for breast cancer but it has a negative safety reputation, especially related to the cardiovascular (CV) system. The fetal estrogen estetrol (E4) might be a new treatment option for patients with advanced breast cancer. It has less interference with liver function and is expected to be less harmful for the CV system compared to other estrogens whereas data from non-clinical and clinical studies suggest anti-tumour effects of E4 in breast tumors.

Currently, a multi-center, open-label, phase I/IIa, dose-escalation Proof of Concept study with E4 is ongoing in Germany in patients with advanced breast cancer (ABCE4 study). The main objectives of this study are to evaluate the safety, the effects on estrogen deficiency symptoms (such as hot flushes, arthralgia, sleep disturbances, bone loss, cognition) and the preliminary anti-tumour activity of E4 in patients with advanced breast cancer.

Cohorts of at least 3 patients will receive doses of 20 mg, 40 mg and 60 mg E4, respectively. Patients will be treated once daily by oral administration for 12 weeks. Postmenopausal women with ER+ advanced breast cancer are eligible for inclusion. In total 9-18 patients will be enrolled at three centers in Germany.

Available data will be presented. Data from the complete Proof of Concept study should give more insight into the potential of E4 as new treatment option for patients with advanced breast cancer.