

Estrogens, Estetrol and Breast Cancer

Herjan JT Coelingh Bennink

Pantarhei Oncology, Zeist, the Netherlands

Scientists, doctors, patients, the lay public and the press all blame estrogens for causing breast cancer (BC), although they rarely distinguish between causing BC or just stimulating the growth of BC. Estrogens are known to stimulate the growth of existing estrogen-receptor positive BC indeed, but estrogens are also an effective treatment of BC under special conditions. This contradictory knowledge is known as the “estrogen paradox”. The data summarised in this presentation demonstrate that high-dose estrogens is an effective treatment of advanced breast cancer more than 5 years after menopause and also after the occurrence of resistance to endocrine anti-estrogen treatment. Essential for efficacy is an extended period of estrogen deprivation before the tumour is subjected to estrogen treatment (the “gap hypothesis”). However, high-dose estrogens have been abandoned for BC treatment due to cardiovascular side-effects.,

Estetrol (E4) may be a new treatment option for patients with advanced breast cancer, since this fetal estrogen has less interference with liver function and is expected to be less harmful for the CV system, whereas data from non-clinical and clinical studies suggest anti-breast tumor effects.

Currently, a phase I/IIA, dose-escalation Proof of Concept study with E4 is ongoing in Germany in postmenopausal patients with advanced ER+ breast cancer and the first results are reassuring both in terms of anti-tumor effects as well as well being.