

T regulatory cells (T-regs) and vascular endothelial growth factor (VEGF): Their relation with estrogen (E2) in premenopausal breast cancer (BC).

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Reproductive function and BC share developmental pathways that are mediated by E2: Modulation of VEGF expression and T-regs proliferation. Both functions are important for embryo implantation, pregnancy maintenance and breast cancer progression. Objective of this study was to evaluate whether E2 suppression with an LH-RH analog was able to down regulate VEGF expression, and to decrease the number of circulating T-regs in premenopausal BC patients with high-risk estrogen receptor positive (ER+) and negative (ER-) early BC. From 04-2003 to 10-2008, 100 premenopausal early BC patients were entered into the study. At baseline, after surgery, and every six months, plasma VEGF and T-regs were measured. Treatment consisted of LH-RH analogue for 5 years, tailored chemotherapy, radiation therapy, and 5-year hormonal therapy in ER+ tumors. Primary end-point was the evaluation of VEGF and T-regs. Secondary end-points were progression-free survival (PFS) and overall survival (OS). Median age 43 years; mean number of positive axillary nodes 3.3; 83% ER+, 17% ER- and PGR-, 20% Her2+, Median KI-67, 33%. After 1 and 5 years, 94% of patients, both ER+ and ER-, were disease-free and had a statistically significant decrease of VEGF ($p < 0.001$) and T-regs ($p < 0.001$). 6% had a disease relapse with VEGF and T-regs increase with respect to baseline values ($p < 0.001$). No unexpected toxicity of chemotherapy was observed, while hot flashes and G1 osteopenia were mild. After a median follow-up of 50 months (range 24-90), 5-year PFS and OS were 94% and 100%, respectively. E2 deprivation with an LH-RH analogue is able to decrease plasma VEGF levels and T-regs in premenopausal high risk ER+ and ER- BC patients. These data show how estrogens, through VEGF modulation and T-Regs proliferation, may be responsible for the worst prognosis that is observed in premenopausal BC patients.

Biography

Francesco Recchia MD has completed his M.D at the age of 24 years from Rome University and postdoctoral studies from University of Texas, MD Anderson Hospital. He is the director of Medical Oncology at The Civilian Hospital Avezzano, affiliated with the University of L'Aquila, Italy. He has published 247 papers in reputed journals and he is serving as an editorial board member in several Oncology journals.