VEGF-A LEVEL AS A PREDICTOR OF BEVACIZUMAB BENEFIT FOR BREAST CANCER: SYSTEMATIC REVIEW WITH META-ANALYSIS

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Aim: Bevacizumab lacks any potential biomarker of benefit, precluding its optimal use for breast cancer therapy. Among the putative candidates, the serum levels of vascular endothelial growth factor-A (VEGF-A) - a target of bevacizumab - has recently called attention as a promising marker. We sought to evaluate the role of VEGF-A levels as a biomarker.

Methods: We searched electronic databases and meeting proceedings for randomised controlled trials (RCTs) comparing the addition of bevacizumab to standard chemotherapy. RCTs were included if outcomes of high and low VEGF-A serum breast cancer patients were presented. Random-effects model were applied to calculate the pooled hazard ratios for event-free survival (EFS), comprising disease recurrence, progression or any-cause death, and overall survival (OS), with respective confidence intervals (95% CI). High and low VEGF-A levels subgroups followed each trial definition, and results were compared using interaction test. Heterogeneity was calculated using Chi-squared test (I²).

Results: Three trials enrolled a total of 3748 patients, with 1713 patients with VEGF-A serum available for assessment, were included. One trial added bevacizumab in adjuvant setting (N = 2591, 1155 for biomarker evaluation) and two as first-line therapy (N = 1157, 558 for biomarker evaluation). Bevacizumab improved EFS of patients with above median VEGF-A serum levels (HR: 0.62; 95% CI 0.49–0.79; P < 0.001; I² = 11%), but not those with below median VEGF-A levels (EFS 0.89; 95% CI 0.71–1.11; P = 0.98; I² = 17%), with relevant differences between these two groups, P for interaction = 0.03. There was no interaction between VEGF-A levels and the study population (adjuvant versus first line therapy). OS data was not available, and therefore data could not be pooled.

Conclusions: The need for a marker of benefit of this expensive therapy medication is an unmet need and better patient selection can improve outcomes and resource use. Serum VEGF-A levels may be a promising marker of bevacizumab activity in breast cancer, either in palliative or adjuvant scenario and further assessment of bevacizumab use in breast cancer should focus on VEGF-A measurement

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