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Bevacizumab in First-Line Treatment of Metastatic Breast Cancer

A Viewpoint by David Miles

Mount Vernon Cancer Centre, Northwood, Middlesex, England

For several decades, the process of angiogenesis has been understood to be a prerequisite for tumour growth and metastasis. Vascular endothelial growth factor (VEGF) is a key angiogenic factor and strategies to target VEGF or its receptor are being evaluated in several tumour types. Bevacizumab, a humanised monoclonal antibody to VEGF, inhibits tumour growth in xenograft models: 'normalisation' of existing vasculature and consequent lowering of oncotic pressure within tumours has also been demonstrated to increase delivery of other agents to tumours providing the rational basis for its combination with other agents.

In early-phase clinical trials in heavily pretreated breast cancer patients, bevacizumab exhibited modest single-agent activity.[1] A pivotal randomised study examined the use of bevacizumab in combination with capecitabine, again in heavily pretreated patients.[2] Though antitumour activity in terms of response rate was significantly higher for the combination regimen than with chemotherapy alone, the primary endpoint of the study, progression-free survival, was not significantly prolonged.[2] The E2100 study described in the accompanying article evaluated the use of bevacizumab in the first-line treatment of metastatic breast cancer. The addition of bevacizumab to weekly paclitaxel increased tumour response rate and importantly, doubled the time to disease progression from ≈6 months to >1 year. Bevacizumab treatment added little to the toxicity of chemotherapy, though as expected, hypertension was noted in about one-fifth of patients and mild proteinuria was evident. The results of this study have lead the European Agency for the Evaluation of Medicinal Products to grant a license for its use in this setting, though the US FDA are currently reviewing source data.

Proof of principle for the utility of anti-angiogenic therapy in breast cancer has been established and results of double-blind, placebo-controlled studies in similar settings to confirm these observations are awaited with interest. ▲

References

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