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Bevacizumab in First-Line Treatment of Metastatic Breast Cancer

A Viewpoint by Xavier Pivot

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Vascular endothelial growth factor (VEGF) is crucial for tumour angiogenesis and thus, the inhibition of circulating VEGF by bevacizumab seems a pertinent approach as an anticancer treatment. Whilst the key impact of bevacizumab is associated with vascular regression, the normalisation of tumour vasculature related to treatment with bevacizumab is also of interest. These changes reduce intratumoural pressure, thereby facilitating tumour exposure to chemotherapy.

The E2100 trial evaluating first-line treatment of metastatic breast cancer with bevacizumab plus paclitaxel versus paclitaxel alone was stopped early, following the recommendation of the Independent Data Monitoring Committee. Median progression-free survival (PFS) was increased by 99% from 6.7 to 13.3 months with the addition of bevacizumab, resulting in a 52% reduction in the risk of disease progression in bevacizumab plus paclitaxel recipients ($p < 0.0001$). The magnitude of this PFS benefit is one of the largest ever seen, especially when compared with randomised trials that led to the registration of chemotherapic agents for metastatic breast cancer, and allowed for registration of bevacizumab for this indication in Europe.

Currently, there are numerous, ongoing phase III trials designed to further evaluate the use of bevacizumab in metastatic breast cancer. These include the AVADO trial, which compares docetaxel with either placebo or bevacizumab; the RIBBON 1 and 2 trials evaluating chemotherapy with or without bevacizumab as first-line treatment and beyond, respectively; and, based on the promising results observed by combining bevacizumab with trastuzumab treatment in a phase I/II trial, the AVEREL trial is investigating the benefits of adding bevacizumab to docetaxel plus trastuzumab in human epidermal growth factor receptor type 2 (HER2)-positive metastatic breast cancer.

Phase III trials investigating the use of bevacizumab in early-stage disease are also ongoing. The E5103 trial is investigating combining bevacizumab with an adjuvant chemotherapy regimen. Similarly, BEATRICE will assess bevacizumab in a subset of patients with triple negative tumour (i.e. HER2, estrogen and progesterone receptor negative) and the NSABP-40 trial will evaluate bevacizumab plus chemotherapy as neoadjuvant treatment.

The registration of bevacizumab for first-line treatment of metastatic breast cancer brings new hope for patients and might pave the way for its extensive use in patients with breast cancer. ▲