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Metastatic breast cancer: Bevacizumab slows progression, but has no impact on survival

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The cancer drug bevacizumab (Avastin) offers only a modest benefit in delaying disease progression in patients with advanced stage breast cancer, according to a systematic review by Cochrane researchers. The researchers assessed the efficacy of bevacizumab in combination with chemotherapy, an established cancer treatment in this indication, and found no overall survival benefit when adding bevacizumab to chemotherapy.

Breast cancer is the most common cause of cancer death among women. If it spreads to other parts of the body it is referred to as "metastatic" and the cancer becomes much more difficult to treat. One promising approach is drugs that target vascular endothelial growth factor (VEGF), a key molecule mediating growth of blood vessels in tumours. At present, trials of drugs that target VEGF are limited to bevacizumab, which is the first drug of this type to be approved for metastatic breast cancer.

To assess the clinical value of bevacizumab in combination with other established chemotherapy drugs, the researchers gathered evidence from seven trials involving a total of 4,032 patients, most of whom had metastatic breast cancer. They found that adding bevacizumab to established drug regimens increased the time to tumour progression or death by between one and six months, depending on the chemotherapy drugs prescribed. However, the researchers found that adding bevacizumab to first- or second-line treatments did not increase overall survival or quality of life.

"At best, adding bevacizumab to standard chemotherapy appears to offer a modest benefit for those with metastatic breast cancer," said lead researcher, Anna Dorothea Wagner, of the Fondation du Centre Pluridisciplinaire d'Oncologie, University Hospital Lausanne, Switzerland. "Whether it can truly be of benefit to the patient is debatable, because it only briefly prolongs progression of the disease. No impact on the patient's overall survival or quality of life has been demonstrated."

According to the researchers, clinical trials testing new drugs for advanced stage breast cancer should follow patients until death in order to understand the impact of new treatments on survival. "The fact that an increase in progression-free survival does not lead to an increase in overall survival suggests that progression-free survival may not be a reliable surrogate for clinical trials in metastatic cancer," said Wagner.

In 2011, the US Food and Drug Administration (FDA) removed breast cancer from indications on the label of bevacizumab, due to concerns about serious side effects and doubts about its benefit in terms of overall survival. By contrast, it is approved for first-line treatment of metastatic breast cancer in Europe, in combination with the cancer drug paclitaxel, as well as in combination with capecitabine for patients with metastatic cancer who are not eligible for treatment with taxanes or anthracyclines.

More information: Wagner AD, Thomssen C, Haerting J, Unverzagt S. Vascular-endothelial-growth-factor (VEGF) targeting therapies for endocrine refractory or resistant metastatic breast cancer. *Cochrane Database of Systematic Reviews* 2012, Issue 7. Art. No.: CD008941. DOI: 10.1002/14651858.CD008941.pub2

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