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## Antiangiogenic therapy: impact on invasion, disease progression, and metastasis.

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### Abstract

Antiangiogenic drugs targeting the VEGF pathway have slowed metastatic disease progression in some patients, leading to progression-free survival (PFS) and overall survival benefits compared with controls. However, the results are more modest than predicted by most preclinical testing and benefits in PFS are frequently not accompanied by overall survival improvements. Questions have emerged about the basis of drug resistance and the limitations of predictive preclinical models, and also about whether the nature of disease progression following antiangiogenic therapy is different to classic cytotoxic therapies—in particular whether therapy may lead to more invasive or metastatic behavior. In addition, because of recent clinical trial failures of antiangiogenic therapy in patients with early-stage disease, and the fact that there are hundreds of trials underway in perioperative neoadjuvant and adjuvant settings, there is now greater awareness about the lack of appropriate preclinical testing that preceded these studies. Improved preclinical assessment of all stages of metastatic disease should be a priority for future antiangiogenic drug discovery and development.

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