

Angiogenesis and cancer

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Angiogenesis, the development of new blood vessels from existing ones, is a complex process that is regulated by pro- and anti-angiogenic factors. Physiological neovascularization takes place during tissue growth and repair, during the female reproductive cycle, and during fetal development. Angiogenesis is also required for tumor growth and metastasis and, therefore, represents an exciting target for cancer treatment. There are two phases in tumor neovascularization, which are separated by the 'angiogenic switch'. Tumoral angiogenesis occurs in a series of complex and interrelated steps. Because of this stepwise process, anti-angiogenic strategies for treatment can be developed against any of several steps in the process. Preclinical as well as clinical evaluation of novel compounds is progressing at a rapid pace. Bevacizumab, a recombinant, humanized monoclonal antibody to vascular endothelial growth factor, a key regulator of tumor angiogenesis, demonstrated potent antitumor activity in preclinical models and has also shown biological activity and clinical benefit in clinical studies in kidney and colorectal carcinoma. Nevertheless, mechanism(s)

that mediate progression in the presence of bevacizumab must still be determined. Stromal and other cell types also play a role in angiogenesis. Identifying the angiogenic pathways after VEGF blockade remains a goal. Furthermore, with bevacizumab's success, several antiangiogenic agents and approaches are currently being evaluated in ongoing clinical trials. PTK/ZK, a new oral targeted therapy designed to block the growth of blood and lymphatic vessels, is active as first-line therapy in patients with metastatic colorectal cancer when combined with FOLFOX chemotherapy (Phase III CONFIRM 1 trial). There is new excitement with the success of anti-angiogenic approaches to treat cancer. Not only patients with advanced disease could benefit from such a strategy. With the development of biomarkers associated with angiogenic tumors and with the availability of angiogenic inhibitors, treating cancer before it becomes symptomatic and anatomically located might be only a matter of time.