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Predictive markers of anti-VEGF and emerging role of angiogenesis inhibitors as immunotherapeutics

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Abstract

The critical role of angiogenesis in promoting tumor growth and metastasis has been well established scientifically, and consequently blocking this pathway as a therapeutic strategy has demonstrated great clinical success for the treatment of cancer. The holy grail however, has been the identification of patients who derive significant survival benefit from this class of agents. Here we attempt to delineate the diverse mechanisms related to anti-VEGF including its role as an anti-vascular, anti-angiogenic or an anti-permeability factor and review the most promising predictive biomarkers interrogated in large clinical trials, that identify patients who may derive significant survival advantage with VEGF inhibition. Lastly, we describe the function of VEGF as an immunomodulator and illustrate the evidence for anti-VEGF in reprogramming the tumor milieu from an immunosuppressive to an immune permissive microenvironment in human cancers, thus elucidating the role of anti-VEGF as an optimal combination partner for immune checkpoint inhibitors.

Keywords: Angiogenesis, immunotherapy, VEGF, CTLA4, PD-L1/PD-1, predictive biomarkers, clinical trials, cancer immunity, inflammation

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