Tivozanib, a selective VEGFR TKI, potently blocks angiogenesis and growth in tumors that express a high level of VEGF-C and are refractory to VEGF-A blockade

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Introduction

Scientific understanding of the role of VEGF-A in tumor angiogenesis has led to the development of specific therapeutic agents, such as bevacizumab, that selectively target VEGF-A. However, clinical trials across multiple cancer types have resulted in limited positive outcomes. VEGF-C is thought to be a potential lymphangiogenic growth factor and plays a role in tumor angiogenesis through VEGFR3. It has also been shown to have some tumor angiogenic activity. Nevertheless, a direct role of VEGF-C in driving tumor angiogenesis has not been established.

To explore the potential of VEGF-C as a driver of tumor angiogenesis, and its implication in developing antiangiogenic therapy, we assessed the activity of tivozanib, a potent and selective TKI for VEGFR1,2 and 3, and a VEGF-A targeted antibody in animal tumor models that exhibit distinct VEGF-C and VEGF-A expression.

Translational potential in human cancer

AVEO’s population-based murine tumor model

VEGF-A high

VEGF-C high

VEGF-C high

VEGF-C high

Translational potential in human cancer

- Marked tumor responses achieving high VEGF-A to low VEGF-C ratios in VEGF-A tumor are sensitive to VEGF-A antibodies

Summary

- A significant portion of human tumors express high-level VEGF-C, suggesting that pan VEGFR TKIs, such as Tivozanib, may have broader activity than agents that selectively target VEGF-A