Accelerated metastasis after short-term treatment with a potent inhibitor of tumor angiogenesis.

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Abstract
Herein we report that the VEGFR/PDGFR kinase inhibitor sunitinib/SU11248 can accelerate metastatic tumor growth and decrease overall survival in mice receiving short-term therapy in various metastasis assays, including after intravenous injection of tumor cells or after removal of primary orthotopically grown tumors. Acceleration of metastasis was also observed in mice receiving sunitinib prior to intravenous implantation of tumor cells, suggesting possible "metastatic conditioning" in multiple organs. Similar findings with additional VEGF receptor tyrosine kinase inhibitors implicate a class-specific effect for such agents. Importantly, these observations of metastatic acceleration were in contrast to the demonstrable antitumor benefits obtained when the same human breast cancer cells, as well as mouse or human melanoma cells, were grown orthotopically as primary tumors and subjected to identical sunitinib treatments.

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