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Investigation of antitumor effects of sorafenib on desmoid tumors

**Background:** Sorafenib is an inhibitor that targets several receptor tyrosine kinases, including vascular endothelial growth factor receptor 2 (VEGFR2) and platelet-derived growth factor receptor (PDGFR). Recently, the antitumor activity of sorafenib has been clinically demonstrated in desmoid tumor (DT) patients; however, its mechanism of action is still unknown.

**Objective:** To investigate sorafenib mechanism of action in DT cells.

**Methods:** A panel of DT cell strains was exposed to increasing concentrations of sorafenib *in vitro* and evaluated for cell growth, migration, invasion, cell cycle, and apoptosis. The expression and activation of VEGFR2, PDGFR- $\beta$  and downstream components were analyzed in DT cells strains by western blot.

**Results:** Sorafenib caused cell growth inhibition in DT cell strains. Interestingly, the induction of apoptosis was observed only in a subset of DT cell strains, indicating that in some DTs cell growth retardation is not due to apoptosis. Sorafenib also decreased DT cell migration and invasion. Furthermore, our results demonstrated that VEGFR2 is not expressed in DT cell strains. PDGFR- $\beta$  is expressed but no basal activation was observed in DTs. Treatment with sorafenib caused significant down-regulation of the activation of ERK, but not MEK.

**Conclusions:** Sorafenib exhibits significant anti-DT activity and elicits apoptosis in a portion of these cell strains. These data suggest that although sorafenib in the clinical context might affect the tumor microenvironment there is also a direct effect on DT cells. Furthermore, our results suggest that the antitumor activity of sorafenib in DTs cells does not occur by targeting the tyrosine kinases VEGFR2 and PDGFR-b but possibly through the inhibition of other unknown tyrosine kinase receptors or directly through blocking ERK.