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Initial studies of Tegatrabetan (BC-2059) in Desmoid Tumor cell strains

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Abstract:

Background: Desmoid tumors (DTs) are rare mesenchymal lesions with high risk for local recurrence. Surgery remains the mainstay treatment; however, this often results in significant treatment-related morbidity and high recurrence rates, suggesting the need for more effective DT treatments. Most DTs commonly feature deregulation of the Wnt pathway. For that reason, the inhibition of Wnt/β-catenin signaling emerges as a potential therapeutic target for these tumors. Therefore, the aim of this study was to investigate the antitumor effect of a novel agent targeting beta catenin stabilization (BC-2059) in DT models.

Methods: A panel of DT cell strains was exposed to increasing concentrations of BC2059 in vitro and evaluated for cell proliferation. Antitumor effects were assessed in vitro by apoptosis, migration, and invasion analysis.

Results: We selected fourteen DT cell strains and two normal cell lines, fibroblasts (NDF-α) and human mesenchymal stem cells (HuMSC), to analyze cell growth after treatment with BC2059. Due to the slow proliferation of DT cells, growth inhibition effects are usually observed only after weeks of treatment; however, BC2059 (doses ranging from 10-500nM) markedly inhibited proliferation of mutated DT cells in only 4 days. Interestingly, no growth inhibitory effects were observed in wild-type DTs. To examine whether anti-proliferative BC2059 effects on DT cell strains were mediated via induced apoptosis, we performed flow cytometric apoptosis analysis of BC2059-treated cells. Our results showed that BC2059 treatment induced apoptosis in the β-catenin mutated DT cells stains. Once more, no significant changes in apoptosis levels were observed in wild-type DT cell strains. We also examined the potential effect of BC2059 on DT cell migration and invasion. The treatment with 100nM of BC2059 for 24h resulted in decreased cell migration and invasion in DT cell strains analyzed.

Conclusions: Our findings suggest that BC2059 has significant antitumor activity against β-catenin mutated DTs, and may comprise an alternative strategy for these tumors' treatment.