WNT PATHWAY INHIBITOR ROLE IN TREATMENT REFRACTORY HEPATOBLASTOMA

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Keywords: Hepatoblastoma, wnt, small molecule inhibitor

Background: Relapsed hepatoblastoma (HB) has a survival rate less than 50% due to limited treatment options. WNT/β-catenin pathway has been shown to have a significant role in liver development and tumorigenesis. Hepatoblastoma has been shown to have high rates of β-catenin mutations and is a candidate for WNT/β-catenin pathway inhibitors. We sought to characterize the role that a novel WNT/β-catenin pathway inhibitor has on hepatoblastoma in vivo.

Materials/Methods: Established HB cell lines and a HB patient derived xenograft cell line were treated with WNT/β-catenin pathway inhibitor, Tegavivint. Cell viability assays were performed to determine half-maximal inhibitory concentration (IC50). Difference in gene expression of WNT/β-catenin pathway after treatment was assessed using quantitative Reverse transcription polymerase chain reaction (qPCR).

Results: Established hepatoblastoma cell lines (Hep T1, Hep G2, HUH-6) and patient derived cell line (HB17) showed decreased beta-catenin expression after Tegavivint treatment after 24 hours. Cell viability assays demonstrated IC50 after 24 hours of Tegavivint treatment of HUH6 at 0.03 μM, Hep T1 at 0.06 μM, Hep G2 at 0.04 μM, and HB17 at 0.76 μM.

Conclusions: We conclude Tegavivint, a novel WNT/β-catenin pathway inhibitor has a role in treatment of relapsed hepatoblastoma. Further evaluation of the mechanism of cell death with Tegavivint is warranted.

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