Inhibition of Ornithine Aminotransferase for Treatment of Hepatocellular Carcinoma. (Hadasit)

code: 8-2010-24

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Need:

Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third leading cause of cancer mortality worldwide. Surgical resection and liver transplantation are considered the only cures for HCC, but benefit only 10-15% of patients. There is a growing need for the development of novel targeted therapies for HCC.

Innovation:

Novel Gabaculine Analogue that has a potential for use of treatment of hepatocellular carcinoma.

Findings:

Ornithine aminotransferase (OAT) is a mitochondrial enzyme that catalyses the interconversion between of ornithine to glutamate. The reaction product, glutamate, is used as a substrate to synthesize glutamine which is a critical for the growth of proliferating cells, synthesis of proteins and nucleotides and providing energy. Using comparative DNA microarray profiling, we have demonstrated that OAT is overexpressed in tumor tissue from spontaneous HCC developing psammomys obesus rat model. In vitro application of Gabaculine (5-amino-1, 3-hexadienyl-carboxylic Acid), a potent naturally occurring potent inhibitor of OAT, significantly suppressed the proliferation of several HCC cell lines. In vivo administration of Gabaculine significantly suppressed tumor growth in Hep3B HCC transplanted athymic mice. Novel Gabaculine Analogue and demonstrated that it significantly suppressed tumor growth in Hep3B HCC transplanted athymic mice.

Indications / Applications:

Hepatocellular carcinoma and other proliferative disorders.

Competitive Advantages:

Currently available treatments are limited and we provide novel targeted therapy for HCC.

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