

## Targeting Liver Cancer Stem Cell Through EpCAM Targeted Therapy Along With Chemotherapy Promote Better Progression In Hepatocellular Carcinoma

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**Abstract:** Chemoresistant and tumor relapse is a major hurdle in the treatment of hepatocellular carcinoma. Majority of conventional chemotherapy fails to treat HCC patients because of numerous factors; in all among cancer stem cell (CSC) is a predominant factor involved in chemoresistant. So, targeting liver cancer stem cell such as EpCAM along with chemotherapeutic drugs have better survival rate for HCC patient.

HuH7 cell line was used as model for hepatocellular carcinoma. HuH7 cells were treated by EpCAM gene silence alone, wnt- $\beta$ catenin signaling inhibitor (XAV939) alone, EpCAM gene silence along with Cisplatin and XAV939 with Cisplatin. The outcomes were studied by Flowcytometry, Spheroid formation assay, Western blot, RT-PCR, Colony forming assay, kinetics and end point assays.

EpCAM gene silenced and XAV939 treated cells shown decrease LCSC marker CD133 expression in Flow cytometry analysis, and reduce expression of ABCG2 gene which is a responsible marker for chemoresistant in RT-PCR analysis than control cells. To support this, EpCAM gene silenced and XAV939 treated cells unable to form colonies in colony forming assay compared to the control cells. Similarly in spheroid formation assay, EpCAM gene silenced cells, XAV939 treated cells and combinations with Cisplatin treated cells were unable to form spheroid, whereas in Cisplatin alone treated cells shown spheroids. In cytotoxicity assay Cisplatin alone and combination with Cisplatin arms shown more cell death than control and only LCSC targeted arms.

These findings were conforming that, conventional chemotherapy kill cancer cells but not cancer stem cells. Chemotherapy combined with EpCAM targeted therapy is enhanced chemo sensitivity and decreased the chance of getting relapsed. This approach might be the suitable option for better prognosis of hepatocellular carcinoma patients.

**Keywords:** Hepatocellular carcinoma, Cancer stem cell, EpCAM, wnt- $\beta$  catenin.

### Article Information

**Conference Proceedings:** World Congress On Cancer Science and Therapy (Bangkok)

**Conference date:** 02-03 December, 2019

[Inovineconferences.com](http://Inovineconferences.com)

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**Citation:** Sivamani G, Sekar S (2019) Targeting Liver Cancer Stem Cell Through EpCAM Targeted Therapy Along With Chemotherapy Promote Better Progression In Hepatocellular Carcinoma. Int J Cancer Treat.

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