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Abstracts

Poster Abstracts

Why targeting vascular endothelial growth factor is not sufficiently effective?

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Introduction: Existing database shows that inhibition of vascular endothelial growth factor (VEGF) signaling may affect tumor growth through several mechanisms. However, clinical studies involving patients with hepatocellular carcinoma (HCC) present various and often disappointing results. We hypothesized that VEGF inhibiting may not be equally effective due to different HHC types.

Methods: Human HCC cells lines Hep 3B, Hep G2, and Sk-hep-1 were cultivated in modified media seeded onto well plates. VEGF-targeting drug Sorafenib 0.05 mg/ml added in study group cultures. General cells count and nuclei morphology were visualized with the TUNEL-staining protocol and cells viewed with a fluorescence microscope (magn. x400). The number of apoptotic cells calculated in percentage of total nuclei. Apoptosis related cytokines were analyzed by Western blotting.

Results: Sorafenib related changes become evident in Hep G2/Hep 3B cell lines after 48 hours of treatment leading to a significant time-dependent reduction of cell numbers of 67.9–83.2% ($p < 0.01$). Cells became sparse, rounded, and detached from the dishes representing morphologic signs of apoptosis. This correlated with activation of caspase-9, caspase-3, and caspase-6. However, Sk-hep-1 cell culture responded much worse with only 36.7–43.7% reduction during same time interval.

Discussion/Conclusion: VEGF-targeted therapy may act through parallel mechanisms that have more or less important role depending on tumor type. In certain malignancies VEGF-targeted therapy has significant activity, whereas in other has no clinical benefit. Our study gives explanation to the fact of variations in clinical response rate of VEGF-targeted therapy. Different subtypes of HCC have different sensitivity to VEGF-targeted therapy.