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Hepatocellular carcinoma (HCC) is the most common primary liver tumor and one of the most common tumors worldwide representing 7.9% of all malignancies (1). Otherwise, hepatic metastases are common in a wide range of malignancies, primarily through the hematogenous mechanism of spread through the portal circulation. However, less than 20% of patients with liver metastases qualify for resection because of tumor size, location, multifocality and/or inadequate hepatic reserve (2). In this context, we have recently focused our interest on In situ delivery system made from 5th generation of dendrimer (G5) diffusible probes composed by NitroImidazole group for targeting hypoxic tumoral cells and site of complexetion of beta emitter 188rhenium.

The aim of the present non-clinical study was to determine the therapeutic efficacy and safety of this agent in an experimental liver cancer model (human HCC cell line HegG2) in mice.

Methods: The experiment agent “ImDendrim” used in this study is consisting of 5th generation poly-L-lysine dendrimer (from Colcom, France) mixed with nitro-imidazole-methyl-1,2,3-triaz36). In vivo protocol was carried out in accordance with the strict French ethical requirements relating to animal testing. 5.0 x 10⁶ cells were subcutaneously injected into mice (from Harlan Laboratories, France with following characteristics: Athymic nude, male, 4-6 weeks of age). Once tumor established, 4 mice lots were treated with a single dose of the test item (1, 2, 2.5 and 3 mCi respectively) compared to control lot. By the end of the study (six weeks post-test compound administration), the tumors were collected for histological analysis.

Results: The treatment was well tolerated. In fact, a significant decrease of tumor volume occurred in all treated groups compared to control group. These results were further confirmed by histological analysis. Large tumor mass only observed in tumor sections from mice in the control group, were disappeared in favor of normal tissues in treated groups.

In conclusion, this novel therapeutic strategy has giving promising experimental results by showing an antitumor activity in this experimental liver cancer model in mice under the tested conditions.

References: