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Preclinical studies of new in situ therapeutic agent derived from dendrimer combined with Nitro-Imidazole and rhenium-188 complex

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Hepatocellular carcinoma (HCC) is the fifth most common neoplasm in the world, and the third most deadly cancer worldwide, with more than 500,000 new cases emerging annually. In this context we have recently focused our interest on *In-situ* anticancer treatment of hepatic tumors using 5th generation polylysine dendrimer as supravector of emitters for β emitter complexes of Nitro-Imidazole probes with rhenium-188 [1].

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: Protocol was carried out in accordance with the strict French ethical requirements relating to animal testing. 5.0×10^6 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 repectivly) 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 anti-tumor activity in this experimental liver cancer model in mice under the tested conditions.

[1]- Belhadj-Tahar and Coll. WO/2015/104589, 2015

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Preclinical studies of new In situ therapeutic agent derived from dendrimer combined with Nitro-Imidazole and rhenium-188 complex (ImDendrim).

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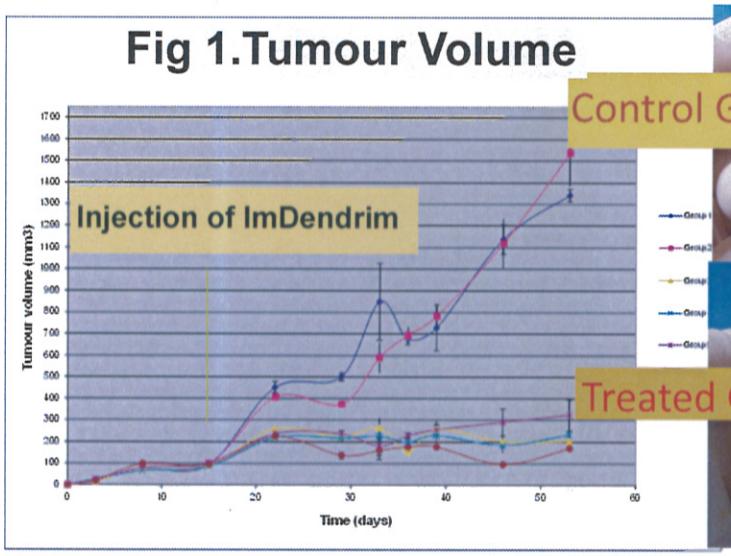
Hepatocellular carcinoma (HCC) is the fifth most common neoplasm in the world, and the third most deadly cancer worldwide, with more than 500,000 new cases emerging annually. In this contexte we have recently focused our interest on In situ anticancer treatment of hepatic tumors using 5th generation polylysine dendrimer as supravector for ß emitter complexes of nitro-Imidazole probes with rhenium-188 [1]. The aim of the present non-clinical study was to determine the therapeutic efficacy and safety of a new *In situ* anticancer agent (ImDendrim from CMP, China) in an experimental liver cancer model in mice.

Methods: Protocol was carried out in accordance with the strict French ethical requirements relating to animal testing. 5.0 x 10^6 human HCC cell line $HegG_2$ were subcutaneously injected into Athymic nude male mice aged 4-6 weeks (from Harlan Laboratories, France). Once tumor established, 4 mice lots were treated with a single dose of the GMP test item (1, 2, 2.5 and 3 mCi repectivly) compared to control lots. By the end of the study (6 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 groups (fig.1).



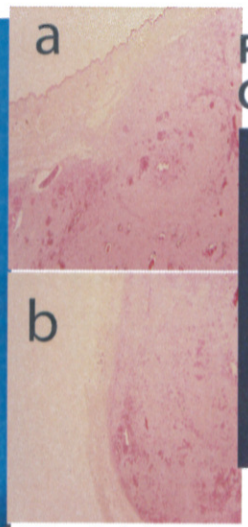


Fig.2 histological analysis

*3hrs post injection

These results were further confirmed by histological analysis. Large tumor mass only observed in tumor sections from mice in the control group (fig.2 a), were disappeared in favor of normal tissues in treated groups(fig.2 b).

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

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