



Lauryl-gemcitabine loaded nanomedicine hydrogel for the local treatment of glioblastoma

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Résumé en
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Glioblastoma (GBM) is one of the greatest challenges in oncology. The standard of care therapy of this highly malignant brain tumor includes surgical resection followed, one month after, by radiotherapy and chemotherapy with Temozolomide. However, GBM still remains incurable mainly because of its anatomical location, high intra- and inter-tumor heterogeneity and intrinsic characteristics that inevitably lead to the formation of recurrences [1]. Considering that 80-90% of GBM recurrences are localized in proximity of resection cavity borders we hypothesized to deliver an injectable nanomedicine hydrogel directly in the tumor resection cavity after surgery in order to obtain a sustained release of the drug. This could avoid the formation of recurrences before starting the conventional treatment. The hydrogel that we have developed and selected is formed of lipid nanocapsules (LNC) loaded with the prodrug Lauroyl-gemcitabine (GemC12), which shows excellent radio-sensitizing properties, could potentiate cancer immunotherapy and has a MGMT-independent mechanism of action [2,3]. This nanomedicine hydrogel is injectable, adapted for brain implantation and able to release the drug over one month in vitro [2]. In vivo, the anti-tumor efficacy studies in a subcutaneous and orthotopic GBM rodent models have shown, respectively, to decrease the tumor growth and increase the survival of the mice after intratumoral injection of the hydrogel compared to the controls. Also, to better mimic the clinical conditions, we have developed and validated a resection model of the GBM orthotopic tumor and on-going anti-tumor efficacy studies after administration of the treatment in the resection cavity are showing promising results. Moreover, short-, mid- and long-term tolerability studies (1 week, 2 months and 6 months) indicated that this system is well tolerated in the brain. In conclusion, we have demonstrated the feasibility, safety and efficiency of the GemC12-LNC hydrogel for the local treatment of GBM. This system, which has a very simple formulation and combines the properties and advantages of nanomedicines and hydrogels, could be considered as a promising platform for the delivery of GemC12 for the local treatment of GBM.

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