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Sunitinib-loaded Chondroitin Sulfate Hydrogels as a Novel Drug-delivery Mechanism for the Treatment of Pancreatic Neuroendocrine Tumors

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BACKGROUND: Pancreatic neuroendocrine tumors (PanNETs) are increasingly common, and experts debate whether small tumors should be resected. Tumor destruction via injection of cytotoxic agents could offer a minimal invasive approach to this controversy. We hypothesize that a new drug delivery system comprising chondroitin sulfate (CS) hydrogels loaded with sunitinib (SUN) suppresses tumor growth in PanNET cells.

METHODS: Injectable hydrogels composed of CS modified with methacrylate groups (MA) were fabricated and loaded with SUN. Loading target was either 200 µg (SUN200-G) or 500 µg (SUN500-G) as well as sham hydrogel with no drug loading (SUN0-G). SUN release from hydrogels was monitored in vitro over time and cytotoxicity induced by the released SUN was evaluated using QGP-1 and BON1 PanNET cell lines. QGP-1 xenografts were developed in 35 mice and directly injected with 25 µL of either SUN200-G, SUN500-G, SUN0-G, 100 µL Sunitinib Malate (SUN-inj) or given 40mg/kg/day oral sunitinib (SUN-oral).

RESULTS: SUN-loaded CSMA hydrogel retained complete in vitro cytotoxicity towards the QGP-1 PanNET and BON-1 PanNET cell lines for 21 days. Mouse xenograft models with QGP-1 PanNETs showed a significant delay in tumor growth in the SUN200/500-G, SUN-inj and SUN-oral groups when compared to SUN0-G ($p=0.0014$). SUN500-G hydrogels induced significantly more tumor necrosis than SUN0-G ($p=0.04$, Table1). There was no difference in tumor growth delay between SUN200/500G, SUN-inj and SUN-oral.

CONCLUSION: Herein we demonstrate that CSMA hydrogels loaded with SUN suppress PanNETs growth. This drug delivery approach represents a novel way to treat PanNETs and other neoplasms via intra-tumoral injection.

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