Co-Administration of rA1M During Lu-177-octreotate Treatment Does Not Interfere with the Therapeutic Effect

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BACKGROUND: PRRT with Lu-177-octreotate has yielded promising results in treatment of patients with metastasized NET, but complete tumor remission is scarce. An approach to achieve better tumor control with increased administered activity is to use radioprotectors that limits the side effects on risk organs. A pharmaceutical candidate of alpha-1-microglobulin (rA1M, RMC-035), a human radical scavenger and antioxidant, with the ability to protect tissues from oxidative stress is a conceivable kidney and hematologic protector during PRRT. This study examines co-infusion of rA1M and Lu-177-octreotate in NET-bearing mice with the aim to investigate if rA1M affects therapeutic response to Lu-177-octreotate administration.

METHODS: The possible effects of rA1M on the change in tumor size after treatment with Lu-177-octreotate were investigated in mice with human small intestine NET, GOT1. The animals were injected with either Lu-177-octreotate, a combination of Lu-177-octreotate and rA1M or rA1M only. Tumor size was measured and followed over time. Furthermore, the biodistribution of Lu-177 after injection of either Lu-177-octreotate, or Lu-177-octreotate and rA1M were studied in mice with human medullary thyroid carcinoma, GOT2. The concentration of Lu-177 was determined in various organs at different time points after injection.

RESULTS: Mice treated with Lu-177-octreotate, or Lu-177-octreotate + rA1M had a strong therapeutic response. The tumor remission and re-growth of the tumors in these two groups were similar. Mice receiving only rA1M showed a continuous
increase in mean tumor volume after the injection. Concentration of Lu-177 in mouse tissue at different time points after co-injection of Lu-177-octreotate and rA1M were not statistically significant different from mice that receiving single injection of Lu-177-octreotate.

**CONCLUSION:** Administration of rA1M simultaneously with Lu-177-octreotate does not interfere with the therapeutic effects of Lu-177-octreotate. rA1M is a promising radioprotector, and further studies should be performed in order to investigate protective renal and hematologic effects of rA1M during PRRT.