Optimization of treatment of neuroendocrine tumors with radiolabeled somatostatin analogues
Eva Forssell-Aronsson, Johan Spetz, Viktor Sandblom, Britta Langen, Khalil Helou, Bo Wångberg, Ola Nilsson

Aim
To present our recent results from optimization of $^{177}$Lu-octreotate therapy of somatostatin receptor (SSTR) expressing neuroendocrine tumors (NET) in animal models.

Conclusion
We have shown several ways to optimize $^{177}$Lu-octreotate therapy in our animal models:
- Fractionated therapy (by up-regulation of SSTR)
- Combination with Hedgehog inhibitor Sonidegib
- Gemcitabine
- Vandetanib

These methods should be clinically tested. Some are suitable for patient-specific treatment planning, while other may be more generally used for all patients.

Introduction
Radiopharmaceuticals have the possibility to cure metastatic disease. $^{177}$Lu-octreotate binds to SSTR often highly expressed by NETs, and is routinely used in major clinics today. Survival is prolonged by ca 4.5 y, although the overall cure rate has not improved much yet.

Methods
Nude mice, xenotransplanted with human SSTR-expressing NETs (GOT1 or GOT2) were injected with suboptimal amounts* of $^{177}$Lu-octreotate alone or together with potential radiosensitizing drugs (e.g. vandetanib, gemcitabine, and a hedgehog inhibitor). Tumors volume was followed with time. Effects on tumor and normal tissues were studied using gene expression microarray, proteomics, and histopathology.

* To be able to detect additive/synergistic effects

Combination with Sonidegib

Combination with Gemcitabine

Combination with Vandetanib

Effect of fractionation

University of Gothenburg
Eva Forssell-Aronsson, professor
Dept of Radiation Physics
Inst of Clinical Sciences
 Sahlgrenska Cancer Center
Sahlgrenska University Hospital
SE 413 45 Gothenburg, SWEDEN

E-mail: eva.forssell_aronsson@radfys.gu.se
Phone: +46 703 722626
Web: www.radfys.gu.se/FA-lab