

Development of AminoMedix™, a Kidney Protective Agent During Peptide Receptor Radionuclide Therapy (PRRT) in Neuroendocrine Cancers

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Background: PRRT using radiolabelled somatostatin analogues shows beneficial results in patients suffering from neuroendocrine tumor (NET). One of the main dose limiting factor in PRRT is the renal reabsorption of radiopeptides to kidney, which may lead to radiation induced nephrotoxicity. The Co-infusion of lysine/arginine lowers renal retention of these radiopeptides by about 40%. Here, we report an agent, (AminoMedix™) reducing the kidney uptake of radiopeptides by 67% without compromising the tumor uptake in mice.

Methods: AminoMedix™ solution contains Amifostine trihydrate, Lysine hydrochloride and Arginine hydrochloride. In this study, we tested combinations of various amounts of all three components and tested the kidney retention of ⁶⁸Ga-octreotide in mice model. The mice were give three intravenous injections of AminoMedix™ solution (200µL) at every 45 min interval and sacrificed 4 h post ⁶⁸Ga-octreotide injection. The ⁶⁸Ga-octreotide injection was administered 30 min after 1st AminoMedix™ injection. The kidney retention of ⁶⁸Ga-octreotide was analyzed using gamma counter. We further evaluated AminoMedix™ solutions effect on tumor uptake in mice bearing pancreatic NET tumor.

Results: The AminoMedix™ composition showed significant reduction in kidney uptake of ⁶⁸Ga-octreotide by 67 % among all various compositions we tested. We compared the kidney protective effect of AminoMedix™ solution with individual components of AminoMedix™, Lysine & Arginine (used in Europe) and 15% Clinisol (used in USA). The uptake of radiolabelled octreotate in somatostatin receptor-expressing normal tissues and tumor was not affected by AminoMedix™ solution.

Conclusion: The AminoMedix™ resulted in maximum reduction of renal retention of ⁶⁸Ga-octreotide. Tumor uptake of radiolabelled octreotate was not affected, resulting in an increased tumor to kidney ratio. More effective kidney protective agents can enhance the safety profile and probably facilitate higher maximum tolerated dose of radiopeptide in PRRT.