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Radiolabelled Somatostatin Analogues for Targeting Somatostatin Receptor Expressing Neuro-EndocrineTumors

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Somatostatin receptor (SSTR)is the biomarkers over-expressed onneuroendocrine tumors (NETs). NETs are embryonal tumors of the sympathetic nervous system derived from the neural crest. NETs are slow growing therefore diagnosed when already metastasized. Radiolabelled somatostatin analoguesDOTATOC/NOC/TATE are used as theranostic agents for SSTR expressing tumors. Cold SST analoguesare generally used as targeted cytostatic drugs to restrict tumor progression. However, radiolabelledSST derivativetherapy act as is targeted cytotoxicdrug due to β-emissions.This therapy is known as Peptide receptor radionuclide therapy (PRRT). The preliminary requirement for radionuclide therapy is that the tumor and metastatic sites should show avidity for thesesomatostatin analogues. We have used Ga-68 DOTATATE/NOC to see avidity, for response evaluation and recurrence of disease. Lu-177DOTATATE/NOC was used for therapy.

Ga-68 was eluted from in-house generator. DOTATATE/NOC labelling was performed at pH 4-4.5 and heating at 95^{o}C for 10 min. However, Lu-177 DOTATATE/NOC was labeled at pH 4.5-5.0 for45min heating.Quality control was done by using TLC scanner with radio-detectors. Diagnostic Ga-68 DOTATATE/NOC was injected (3-5 mCi) and images were acquired after 45-60 min using PET/CT scanner. For therapy,100-200 mCi dose, based on body weight, wasslowly infused intravenously. Before therapy kidney and liver functions were evaluated. Post therapy scan was taken after 24h using imagable γ-photos of Lu-177, 113 keV (6.4%) and 208 keV (11 %).Nausea, vomiting, abdominal discomfort and mild hematological toxicity were observed in patients andgradually subsided.Earlier, nephrotoxicity was the major concern duetore-absorption of radiolabelled peptide in the renal tubuli. Positively charged amino acid infusion significantly reducedthe renal toxicity.

PRRT delivers continuous radiation with a decreasing dose-rate due to the decay of attached radionuclide.Tumour tissue is benefited by cytotoxic effect of beta particles and spares adjacent normal tissues due tolow penetration of beta particles. The SSTR being G-protein coupled receptors (GPCR), the receptor-mediated internalization and intracellular retention of a radiolabeled peptide into the endosomes is the biologic basis for this therapy.