Canadian Radiotheranostics Leaders' Summit 2025

Abstract Submission

Title: Improved CXCR4-targeted radioligand therapy in neuroendocrine prostate cancer

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Abstract:

Purpose:
Neuroendocrine prostate cancer (NEPC) is an aggressive subtype of prostate cancer and patients usually have a poor prognosis. We have confirmed c-x-c chemokine receptor 4 (CXCR4) expression in different NEPC patient-derived-xenografts (NEPC PDX) models suggesting its utility for radioligand targeted therapy. A lutetium 177 labeled CXCR4-targeting radioligand resulted in modrate tumor growth inhibition in a murine model. Therefore, novel CXCR4-targeting radioligands coupled to albumin binding moieties were designed to improve tumor uptake. In this study, we evaluated the tumor inhibition and hematoxicity profile of [177Lu]Lu-BL34T1 in mice.

Materials and Methods:
A CXCR4-targeting peptide carrying an albumin binding moiety (BL34T1) was radiolabeled with lutetium-177. LTL331R NEPC PDX tumor-bearing mice (n= 8-10) were randomized and injected with 10 MBq, 20 MBq, 40 MBq or NaCl control. Tumor growth and blood cell counts were monitored longitudinally. Experimental endopoint was determine when tumor volume was >1200 mm3,

mice lost >15% body weight or any behaivoral changes were observed.

Results:
[177Lu]Lu-BL34 resulted in a dose-dependent tumor growth inhibition in LTL331R-tumor bearing mice. At day 8, the % tumor growth inhibition (%TGI) in comparison to the control group was 36, 43 and 57% for mice injected with 10, 20 or 40 MBq of the radioligand, respectively. Exponential tumor regrowth was observed in all treated groups at different times. Longer median overall survival was determined for mice injected with 10 MBq (38.5 days), 20 MBq (81 days) and 40 MBq (128.5 days) in comparison to the control group (21 days) ($p<0.001$). Notably, no significant changes in body weight, platelets, leukocytes or erythrocytes was observed among the different groups.

Conclusions:
This preclinical therapy study shows that [177Lu]Lu-BL34T1 has potent tumor inhibition effect in a NEPC PDX model without significant renal and hematological toxicities. Future studies will further investigate potential hematoxicity in a humanized murine model.