Canadian Radiotheranostics Leaders' Summit 2025
Abstract Submission

Title: [225Ac]Ac/[155Tb]Tb-J3-Panitumumab: A Targeted Alpha Therapy and SPECT/CT Theranostic for EGFR Expressing Breast Cancer

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Abstract:

Epidermal growth factor receptors (EGFR) are overexpressed in 50 – 90% of triple negative breast cancers, an aggressive form of breast cancer with poor prognosis and little methods for targeted treatment. Therefore, it is an attractive target for developing theranostic radioimmunoconjugates (RIC) utilizing the anti-EGFR monoclonal antibody Panitumumab (Vectibix, PmAb). Isotopes of interest are 225Ac, a radionuclide used in targeted alpha therapy with remarkable clinical efficacy and 155Tb, a SPECT radionuclide that can be used as the imaging partner for 225Ac. The novel chelator J3, an isothiocyanate derivative of the Crown chelator, was synthesized to enable antibody conjugation while exhibiting efficient room temperature labeling of 225Ac3+, 155Tb3+ and other radio-lanthanides. The novel RICs 225Ac-J3/DOTA-PmAb IgG and antibody fragment 225Ac-J3/DOTA-PmAb f(ab')2 were synthesized and injected into female NRG mice bearing EGFR expressing MDA-MB-468 tumours to evaluate stability and distribution in-vivo. In all four RICs, good tumour accumulation and low background uptake was observed. IgG RICs showed low uptake to healthy organs and the uptake between J3 and DOTA conjugates are overall similar (at 7 days, tumour uptake of 225Ac-J3-PmAb was 44.16 ± 14.23 injected activity/g (%IA/g) and for 225Ac-DOTA-PmAb was 28.84 ± 4.87 %IA/g). While f(ab)'2 RICs showed faster blood clearance and lower tumour to background ratios. 225Ac-J3-PmAb f (ab)'2 showed higher uptake in kidneys and spleen compared to it's DOTA counterpart. Preliminary labelling and cell uptake studies were performed with 155Tb-J3-PmAb IgG as well to evaluate the binding affinity. Overall, the results highlight the potential of panitumumab RICs towards the treatment or imaging for triple negative breast cancer.