Therapeutic Combination of Radiolabeled CLR1404 with External Beam Radiation in Head and Neck Cancer Murine Xenograft Models

Abstract #851


Introduction

• Radiation therapy is a central treatment modality for head and neck cancer (HNC). Although significant technical advances have been made in delivering highly conformal radiation, normal tissue toxicity remains dose limiting.

• Targeted radionuclide therapy (TRT) is an attractive cancer treatment approach that employs radiolabeled molecules to specifically deliver radiation to primary and metastatic tumors.

• CLR1404 is a radiolabeled phospholipid ether analog with theranostic potential as a PET imaging agent (CLR 124, labeled with I-124) and as a radiotherapy agent (CLR 131, labeled with I-131). CLR1404 exhibits preferential uptake in human cancers and provides tumor-selective internal delivery of radiation to complement external beam radiation (XRT) in the treatment of cancer.

• We hypothesized that TRT combined with reduced-dose XRT could reduce the normal tissue toxicity profile compared with high dose XRT alone.

• In this study, we investigated the anti-tumor effect of CLR 131 in combination with external beam radiation (XRT) in HNC.

CLR1404 analogs

CLR1404

CLR1501

CLR 124

CLR 131

Reference


Results

• Confirmed CLR1501 uptake in 20 HNC cell lines in vitro in conjunction with fluorescence microscopy and flow cytometry.

• Confirmed CLR 124 uptake and retention in 12 HNC xenograft and PDX mouse models in vivo PET/CT imaging.

• Significant tumor uptake and retention of CLR 124 with limited retention in normal tissues.

• Enhanced tumor growth inhibition with CLR 131 combined with fractionated XRT in 6 HNC xenograft models compared with single modality treatment.

Conclusion

• In this study, we demonstrate uptake of CLR 131 across multiple HNC cell lines and xenograft models with enhanced anti-tumor effects when CLR 131 is combined with XRT.

• These results suggest the potential value of TRT via CLR 131 combined with reduced dose external beam XRT in HNC patients that will be further tested in a phase I clinical trial at UW.

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