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

Abstract #851

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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 — X-(CH2)18OPOCH2CH2NMe3 (O⊖)

CLR1501 — X = Fluorescent analog

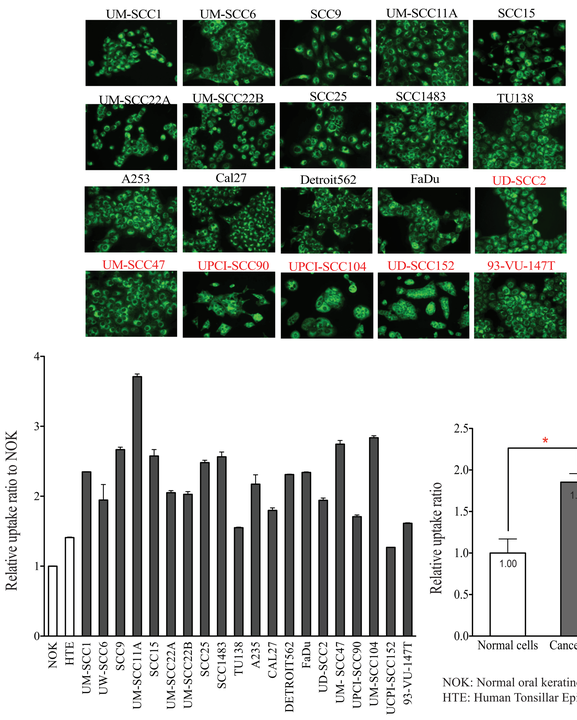
CLR 124 — X = ^{124}I — Radioisostere; PET imaging

CLR 131 — X = ^{131}I — Radioisostere; molecular radiotherapeutic

Reference

Alkylphosphocholine Analogs for Broad-Spectrum Cancer Imaging and Therapy. JP Weichert, PA Clark, IK Kandela, et al. ***Sci Transl Med*** 2014 ; 6(240):240-275

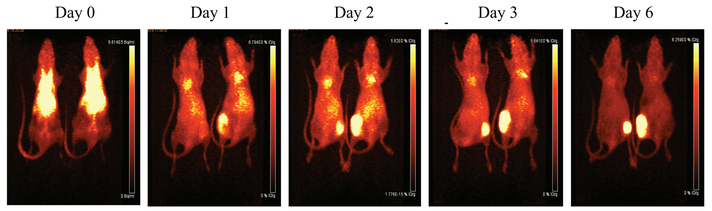
CLR1501 uptake in 20 Cell lines



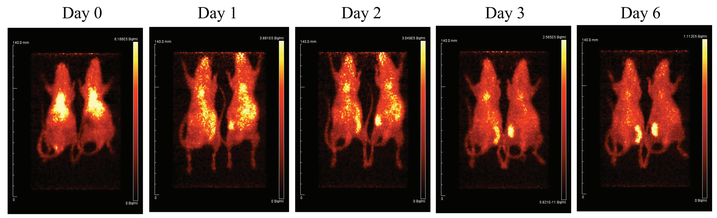
NOK: Normal oral keratinocytes.
HTE: Human Tonsillar Epithelial

CLR 124 uptake in xenograft models

Cell line xenograft --TU138

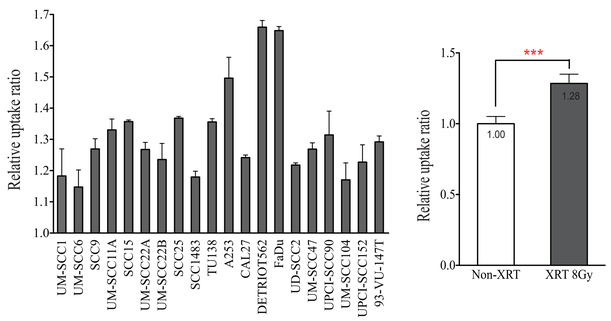


Patience-Derived Xenograft--UW#22

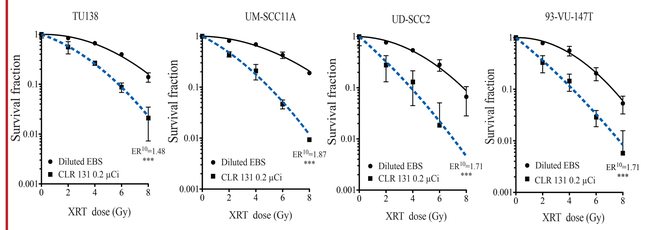


Uptake and prolonged retention of CLR 124 in TU138 and UW#22 tumor xenografts showing high ratios of tumor to normal tissue concentration. 12 head and neck tumor xenografts have been studied with favorable results to date.

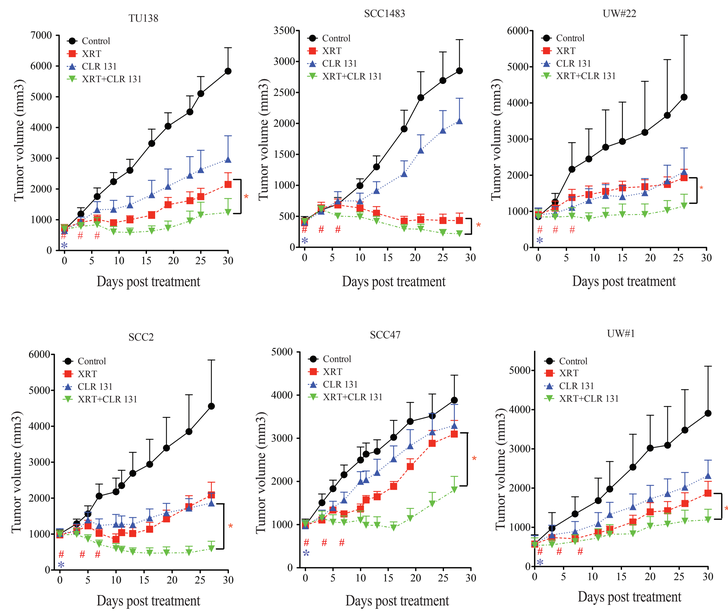
CLR1501 uptake in irradiated cells



Combining CLR 131 with XRT *in vitro*



Combining CLR 131 with XRT *in vivo*



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 via 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

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• 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

Acknowledgements

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