Introduction

- Upwards of 50% of cancer patients will receive radiation during the course of their treatment, mostly through a fractionated dosing schedule.
- Labcorp Drug Development has a wealth of data across syngeneic models employing a single dose of focal radiation. To bolster this data set, fractionated dosing regimens were employed in the CT26, MC38, E.67-OVA and EMT-6 models to compare response to bolus focal radiation therapy.
- These more translationally relevant dosing regimens produce moderate responses that more accurately reflect the clinical landscape and provide a more viable framework for interrogating rational combination strategies in preclinical development.

Methods

- CT26 and EMT-6 cells were implanted subcutaneously or in the mammary fat pad, respectively, of female BALB/cAnNHsd mice. CT26, E.67-OVA and B16F10 cells were implanted subcutaneously in C57BL/6J or C57BL/6J/NHsd mice. Mice were staged into treatment groups when the mean tumor volume was ~100mm³. Tumor growth changes were tracked by caliper measurements.
- All animal work was performed in an AAALAC-accredited facility, in alignment with applicable animal welfare regulations and with predetermined humane euthanasia criteria on all studies.
- Image-guided irradiation was performed under 1-2% isoflurane anesthesia on the Small Animal Radiation Research Platform (SARRP; Xstrahl Inc., Suwanee, GA). Treatment was delivered at 220 kV and 13.0 mA using an appropriately sized collimator to the total indicated dose (in Gray; Gy) in two equally weighted beams.

Conclusions and Next Steps

- Moderately responsive treatment regimens of bolus and fractionated focal radiation were identified for the five models tested.
- No difference in overall tumor growth was seen between bolus and fractionated dose regimens in any model tested.
- These dose regimens are well suited for combination strategies.
- Next steps include assessing differences in combination activity between bolus and fractionated radiation as well as differences in the tumor microenvironment under these conditions.