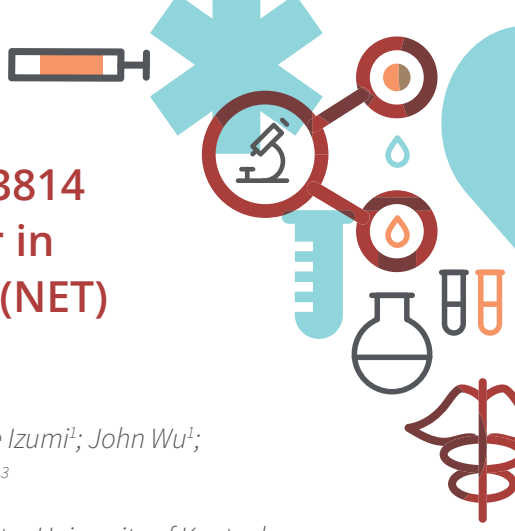

# B-7

## Antitumor Efficacy of M3814 as a Radiation Sensitizer in Neuroendocrine Tumor (NET) Preclinical Models

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**BACKGROUND:** M3814, a DNA-dependent Protein Kinase Inhibitor (DNA-PKi), is known to potentiate the effects of Ionizing Radiation (IR) in various solid tumor in-vivo models. M3814 inhibits DNA damage repair mechanisms. Currently antitumor efficacy of M3814 in NETs is unknown.

**METHODS:** The efficacy of M3814 in combination with external beam radiation (IR) was evaluated in the QGP and BON invitro cell line model as well as QGP (pancreatic NET cell line xenograft) mouse model. Tumor cells were injected s.c. into athymic nude mice for incubation. They were harvested once they attained a large size, they were then dissected and re-implanted into athymic mice. This was done so that the implanted tumor tissue was of equal size. Treatment started when palpable tumors were established (200-300 mm3). M3814 was given orally 30 minutes prior to irradiation. Each mouse was irradiated with 2 gray fractions for 4 consecutive days. IR was applied using a radiation therapy device for small rodents calibrated to deliver 2 Gy. Mice were randomized into 4 groups; XRT alone, M3814 alone, Placebo and XRT+ M3814 combination.

**RESULTS:** Both XRT and XRT+M3814 group showed anti-tumor activity, however, the combination group showed marked anti-tumor activity at both 2 and 3 weeks post-treatment. Of note, the tumors treated with XRT+M3814 were also visibly less vascular as compared to XRT alone and placebo. (Images will be provided in the poster). M3814 alone had no effect on tumor as expected. Both

XRT and XRT+M3814 groups noted post-treatment decline in the mice weight, however, weight change was similar between XRT and XRT+M3814 groups.

**CONCLUSION:** M3814 is a potential radiation sensitizer in preclinical neuroendocrine models. Strong antitumor activity was observed in BON and QGP invitro clonogenic assay and QGP xenograft in vivo model with marked reduction of tumor growth on application of 2-Gy fractions for 4 days with oral M3814.