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A Single-Centre Pilot Study for Radiosensitization of Everolimus with External Beam Radiotherapy for the Treatment of Metastatic Neuroendocrine Liver Metastasis

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BACKGROUND: Liver metastases from neuroendocrine tumors (NELM) are common. Given the benefit of everolimus (E) in patients with neuroendocrine tumors and its additive effect to radiotherapy (RT) in other histologies, this study evaluated safety and efficacy of concurrent E with RT for NELM.

METHODS: Prospective study of 14 patients with < 4 NELM, progressing on standard therapy, treated with E for 28 days prior to, concurrent with, and 14 days following RT. A safety run-in of 2 patients at E 2.5 mg daily, then 5 mg daily were completed prior to treating 10 patients with 7.5 mg daily. RT was delivered using either conventional radiation (cRT) 30Gy in 10 fractions or stereotactic ablative radiation (SABR) 35-60 Gy in 3-5 fractions. Per lesion response was evaluated per RECIST v1.1, and toxicity per the CTCAE v4.03.

RESULTS: 40 NELM were treated in 14 patients (7 male and 7 female), with a median age of 63 (47-88). Primaries included lung (4), small bowel (6), colorectal (3) and renal (1); Gr.I/typical lung (4) and Gr.II/atypical lung (10). Median radiation dose delivered (BED_{10}) was 72Gy (range 39-180). The overall response rate (ORR) was 33%; no patients developed progression at a treated NELM in the 12 month follow-up period. Median change in size per metastasis was -23% (-100% to 7%). 1 patient developed pseudoprogression. Median time to best response was 9 months.
One patient at the 7.5mg dose discontinued E post-RT due to Grade 2 thrombocytopenia, and one patient at the 7.5mg dose had Grade 3 hypertension which resolved after completing E.

**CONCLUSION:** Concurrent E and liver RT is safe. No patients developed progression of their treated NELM in the 12 months post treatment; further follow-up is required to determine long-term control. Combination E and RT may be an option for patients with low-volume NELM; further investigation is warranted for this promising approach.

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