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Liver-directed therapy for metastatic neuroendocrine carcinoma and grade 3 well-differentiated neuroendocrine tumors

Colin Doyle[1]; Razan Ali[1]; Erik Mittra, MD, PhD[2]; Anna Mench, PhD, DABR[2]; Celeste Winters, PhD, DABR, DABSNM[2].

[1]School of Medicine, Oregon Health and Sciences University; [2]Department of Diagnostic Radiology, Oregon Health and Sciences University.

BACKGROUND

Lu177-DOTATATE has been used to treat GEP-NETs since 2018, however a strong correlation between dosimetry results and hematopoietic and nephrological toxicities has not yet been established. This study aims to investigate the relationship between these toxicities and absorbed dose for patients treated with Lu177-DOTATATE at a single institution.

METHODS

Post-therapy dosimetry was performed on 11 patients using quantitative SPECT/CT acquisitions. Ten patients had imaging at 4-, 24-, 48-, and 72-hours post-injection, and one patient had imaging at 4- and 72-hours. Absorbed doses to the kidneys and representative regions of lumbar bone marrow were calculated using organ-level dosimetry (MIM Software Inc., Cleveland, OH). Dosimetry was performed due to re-treatment (7 patients) or due to reduced kidney function (4 patients). Total dose was estimated using the calculated mGy/GBq and the cumulative treatment activity. Pre-therapy baseline lab results were compared to blood labs at an average of 32 days after treatment and kidney labs at an average of 115 days after treatment. Spearman's rank correlation coefficient with Bonferroni correction was used to assess dose-response relationships.

RESULTS

Table 1: Summary Statistics: Administered Activity and Absorbed Dose to the Bone Marrow and Kidneys (Gy/GBq)

Parameters	Range	Mean	Standard Deviation
Cycle 1 Administered Activity (GBq)	3.78 - 7.58	6.91	1.17
Bone Marrow Dose (Gy/GBq)	0.02 – 0.17	0.06	0.04
Kidney Dose (Gy/GBq)	0.25 – 1.21	0.47	0.26

Average bone marrow dose was 0.06 Gy/GBq (range: 0.02 – 0.17 Gy/GBq), and average kidney dose was 0.47 Gy/GBq (range: 0.25 - 1.21 Gy/GBq). Conservative toxicity limits were exceeded for cumulative bone marrow dose (2 Gy) in two patients, and cumulative kidney dose (23 Gy) in four retreatment patients.

Significant correlations were found between bone marrow dose and both white blood cell count reduction ($r_s = -0.86$, $p < 0.01$) and platelet count reduction ($r_s = -0.89$, $p < 0.001$). No significant relationships were found for serum creatinine or hemoglobin.

CONCLUSIONS

Although accepted tolerance doses were exceeded for bone marrow (n=2) and kidneys (n=4), no treatment emergent G3/G4 toxicities were observed. A significant relationship was found between absorbed dose to the bone marrow and both platelet and white cell count reduction at ~1 month after treatment. No relationship was found between kidney dose and serum creatinine; however, the follow-up period may have been too short to see long-term effects.

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