C-21

Effect of Absorbed Dose on Toxicity and Tumor Response of Lu-177-DOTATATE With Olaparib in Gastroenteropancreatic Neuroendocrine Patients: Preliminary Results

Jaydira del Rivero[1], Inna Shamis[1], Joy Zou[1], Baris Turkbey[1], Jorge Carrasquillo[1,2], Roberto Maass-Moreno[3], Esther Mena[1], Liza Lindenberg[1], Clara Chen[3], Corina Millo[3], Peter Herscovitch[3], Peter Choyke[1], Karel Pacak[4], Frank I. Lin[1].

[1]Center for Cancer Research, National Cancer Institute, Bethesda, MD; [2]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY; [3]Clinical Center, National Institutes of Health, Bethesda, MD; [4]Eunice Kennedy Shriver National Institute of Child and Human Development, Bethesda, MD.

BACKGROUND

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are somatostatin receptor (SSTR) expressing tumors treated with Lu-177-DOTATATE. Olaparib is a poly-ADP-ribose polymerase inhibitor that blocks single-stranded DNA repair which may synergize with Lu-177-DOTATATE for both efficacy and toxicity. We present in-progress dosimetry results of a phase 1/2 trial testing this combination in metastatic GEP-NET.

METHODS

Three quantitative SPECT/CT scans (4, 24, 48 hours post-infusion) are performed in NCT04086485, a 3+3 dose escalation phase 1/2 study evaluating Lu-177-DOTATATE + olaparib. Lu-177-DOTATATE is given at fixed 200 mCi x 4 cycles while olaparib is escalated from 50mg to 100mg, 200mg, and 300mg bid. Dosimetry was performed using MIM's SurePlan MRT workflow. Regions of interest (ROIs) are drawn around all major organs and select tumors by an experienced Nuclear Medicine physician using MIM's automatic segmentation and PET Edge tool. Integrated time activity curves were obtained using both MIM's fitting functions and trapezoidal integration. The latter data and the voxel S-value convolution method in SurePlan was used to calculate absorbed doses. CT scans obtained at baseline, post 2-cycles, and post 4-cycles were used for RECIST tumor measurements.

RESULTS

By April 2024, 11 patients were treated (6 patients with 4 cycles, 3 with 3 cycles, and 2 with 1 cycle). Absorbed doses calculated with trapezoidal integration yielded results that were on average 34% higher than best fit method. For the 6 patients who completed therapy, 62 tumors lesions were contoured, of which 23 were official RECIST measurable lesions. For these 62 tumors, absorbed dose over all 4 cycles averaged 51.86 Gy (range: 0.77 to 248.85 Gy) per lesion. Per cycle average dose decreased over time (Cycles 1-4: 15.91, 13.57, 12.36, 11.29 Gy, respectively). No correlation was found between total absorbed dose or olaparib dose with change in RECIST diameter at studied re-staging time points. For toxicity, 3/9 (33%) evaluable patients had grade 1 creatinine elevation with average absorbed doses of 13.35 Gy (left) and 11.91 Gy (right) to kidneys, compared to 12.79 Gy and 11.02 Gy in the other 6 patients. One patient (11%) had grade 1 transaminase elevation with 5.85 Gy to the liver, compared to 25.14 Gy (range: 5.85 to 53.13 Gy) in others.

CONCLUSIONS

Preliminary data suggests that absorbed doses calculated via 3 time-point dosimetry do not correlate with tumor response or organ toxicity after 2 or 4 cycles in patients treated with Lu-177-DOTATATE and olaparib.

ABSTRACT ID 28545