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Ratio of total uptake volume on DOTATATE vs FDG PET as a predictive marker of treatment efficacy of Lu-177-DOTATATE in metastatic pheochromocytoma

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BACKGROUND

Pheochromocytoma/Paraganglioma (PPGL) are rare neuroendocrine tumors that expresses somatostatin receptors (SSTR) and can be treated with radiolabeled somatostatin analogues such as Lu-177-DOTATATE. Ga-68-DOTATATE PET scans show the distribution and density of SSTR+ tumors, and F-18-FDG PET scans show hypermetabolism in lesions. Total uptake volumes (TUV) for each respective scan can be obtained consistently and semi-automatically using standardized workflow in imaging software such as MIM, and the relative TUV ratio of the DOTATATE vs FDG scans is obtained and analyzed in this study.

METHODS

F-18-FDG and Ga-68-DOTATATE PET scans are performed as per the phase 2 clinical trial evaluating the use of Lu-177-DOTATATE in patients with metastatic pheochromocytoma (NCT03206060). Per the study's protocol, FDG (10 mCi) and DOTATATE (6 mCi) PET scans are obtained at baseline. The primary clinical end point is progression free survival (PFS). A workflow was built in MIM Software where lesions are automatically contoured into regions of interest (ROIs) using a SUV threshold (that was arbitrarily determined to screen out most physiologic uptake) of > 5.0 for the FDG and > 23.0 for the DOTATATE PET scans. The resultant ROIs were manually reviewed by a trained Nuclear Medicine physician and adjusted as needed. A ratio of the TUV from the DOTATATE over the FDG PET scans was then calculated and used for this analysis.

RESULTS

Interobserver variability evaluation of three blinded independent Nuclear Medicine physician readers showed the variability in TUV obtained using the semi-automated MIM workflow was less than 10%. On average, the time required to perform a TUV calculation was 3-5 minutes per scan. Thirty-six patients from NCT03206060 are included in this analysis. The ratio of the DOTATATE SUV to FDG SUV ranged from 0.22 (uptake on FDG scan > DOTATATE) to 4911 (uptake on DOTATATE >> FDG scan). The mean PFS is 21.0 and mean OS is 31.0 months for all patients. Using a ratio of 2.0 as a cutoff, patients whose TUV ratio is < 2.0 (n=13) have a mean PFS of 17 months and OS of 26 months while those having a ratio of > 2.0 (n=23) have a mean PFS of 23.0 and OS of 35 months. The c-index between DOTATATE-FDG TUV ratio and PFS is 0.693 (p=0.002), and is 0.674 (p=.045) between TUV and OS.

CONCLUSIONS

The TUV ratio of DOTATATE PET over the FDG PET reflects underlying tumor biology and may be used as a predictive marker of treatment efficacy of Lu-177-DOTATATE.

ABSTRACT ID 23658