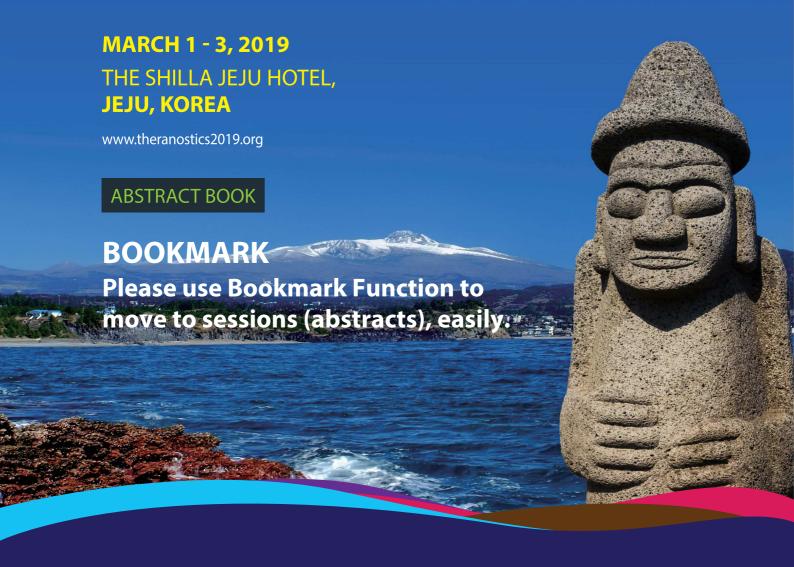


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Prognostic Validity of Dual Tracer PET/CT in the PRRT Enrollment of GEP-NET Patients

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AIM: In 2017, Chan et al. have been developed a grading scheme ("NET-PET" grade) for dual SSTRI/FDG PET reporting in patients affected by metastatic Gastroenteropancreatic-Neuroendocrine Tumors (GEP-NETs) that summarizes the information provided in both scans by a single parameter.

The aim of our work was to assess the validity of NET-PET grade as a prognostic imaging biomarker in metastatic GEP-NETs patients that underwent peptide-radionuclide-receptor-therapy (PRRT).

METHODS: 30 GEP-NET metastatic patients (13 F and 18 M; mean age: 61 years- range 27-80) undergoing both 18F-FDG and 68Ga-DOTATOC PET/CT prior PRRT were retrospectively included in the analysis. Tumors were histologically classified as foregut-GEP-NET (all patients had pancreatic-NETs) in 17 patients, and midgut-GEP-NET (1 gastric, 2 duodenal, 10 small intestinal and 1 colorectal-NET) in 14 patients. Moreover, based on WHO 2010 GEP-NET classification, the patients were classified into 3 groups: 1) G1 (Ki67 <3); 2) G2 (Ki67 from 3 to 20) and 3) G3 (Ki67 >20). Before the PRRT, all patients underwent SSTRI PET/CT (68Ga-DOTATOC) and 18F-FDG PET/CT to detect the presence of somatostatin receptors and the metabolic activity of the disease, respectively. The cohort of patients was graded with the "NET-PET grade" that uses a visual evidence scale (ve): a grade of P1 indicating purely SSTRI-avid disease without FDG uptake in any lesions, and P5 indicating the presence of significant FDG ve+ /SSTRI ve-. Based on the "NET-PET grade", the patients were divided into 3 group: 1) patients that will suitable for treatment with 177Lu-DOTATOC alone (p1-p4a); 2) patients in whom 177Lu-DOTATOC may have a role in the treatment but they are need of other therapy; (p4b) 3) patients that don't unlikely to benefit from treatment (p5). To verify the hypothesis, 3 days after the PRRT, the patients underwent post-therapy Whole-Body (pt-WBS) to assess the radiopharmaceutical biodistribution of 177Lu-DOTATOC and the uptake of the 3 major lesions.

RESULTS: Applying WHO 2010 classification, 5 subjects were graded as G1, 21 as G2 (7 of them with ki67 > 10) and 5 as G3. When the "NET-PET grade" was applied, 12 subjects were graded as P1, 18 as P2-4a, 0 as P4b and 1 as P5. According to the WHO 2010 classification, G3 patients should be treated with chemotherapy. The above mentioned G3 patients, on the other hand, were graded as p2a (2/5), p2b (2/5) and p3a (1/5) by "NET-PET score". Based on "NET-PET score" results, the patients underwent PRRT. Performing pt-WBS three days before PRRT, for all the patients we observed in all three major lesions an intense uptake of 177Lu DOTATOC. On the

other hand, in 1 patient affected by midgut-NET that were graded G2 (Ki67 12%) by Who 2010 GEP-NET classification, PRRT was not successful. Based on NET-PET score assessment, the above-mentioned patient was graded as p5.

CONCLUSION: Our experience suggests and confirmed the NET-PET score can be reliably considered as support for tailored treatment approach, by identifying patients affected by metastatic GEP-NET that might benefit from PRRT or not.