Pre-therapy extrahepatic ^{68}Ga -DOTATATE avid tumor burden is associated with shortterm clinical outcomes of ^{177}Lu -DOTATATE in advanced metastatic gastroenteropancreatic neuroendocrine tumors

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Research Article

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Abstract

Lutetium-177 (^{177}Lu)-DOTATATE is an effective systemic therapy for metastatic somatostatin receptor positive neuroendocrine tumors (NETs). Here we report our experience with the use of pre-therapy ^{68}Ga -DOTATATE PET as prognostic marker for short-term clinical outcomes of ^{177}Lu -DOTATATE therapy in patients with advanced NETs.

Materials and methods: We retrospectively reviewed patients who received at least one dose of ^{177}Lu -DOTATATE between Dec. 2016 and July 2019 at our institution. 50 patients (63.6 ± 10.0 years) with advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who had pre-therapy ^{68}Ga -DOTATATE PET were included in the analysis. ^{68}Ga -DOTATATE avid tumor volumes were determined automatically using an SUV thresholding approach. Total and extrahepatic ^{68}Ga -DOTATATE avid tumor volumes were measured and dichotomized into large and small tumor volume groups. Association with progression free survival (PFS) and overall survival (OS) were determined at median follow up of 32 months by Kaplan-Meier survival analysis with Log-Rank test.

Results: During follow up, 38 patients (76%) had disease progression and 15 patients (30%) died. Kaplan-Meier analysis of PFS in GEP-NETs patients showed that smaller extrahepatic ^{68}Ga -DOTATATE avid tumor volume ($<140\text{ mL}$) is associated with significantly longer PFS (Median PFS 29.0 ± 6.7 months vs 9.0 ± 1.7 months, $P = 0.0001$). This trend in PFS is less prominent when total ^{68}Ga -DOTATATE avid tumor volume is analyzed. Similarly, Kaplan-Meier analysis of OS found that GEP-NETs patients with smaller extrahepatic ^{68}Ga -DOTATATE avid tumor volume ($<150\text{ mL}$) is associated with significantly longer OS (Median OS not reached vs 44.0 ± 12.3 months, $P = 0.002$). This association with OS is not statistically significant when total ^{68}Ga -DOTATATE avid tumor volume is analyzed. When ^{68}Ga -DOTATATE avid hepatic tumor volume is grouped into low ($<500\text{ mL}$), medium ($500\text{-}1000\text{ mL}$) and large ($>1000\text{ mL}$) tumor volumes, no statistically significant difference in PFS is observed, $P = 0.19$. The accuracy of extrahepatic ^{68}Ga -DOTATATE avid tumor volume as prognostic marker for PFS and OS at 32 months are moderate at 58% and 72%.

Conclusions: Smaller extrahepatic ^{68}Ga -DOTATATE avid tumor volumes are associated with longer PFS and OS following ^{177}Lu -DOTATATE treatment in patients with advanced GEP-NETs. The accuracy of extrahepatic ^{68}Ga -DOTATATE avid tumor volume as prognostic marker for PFS and OS at 32 months are moderate, which may limit its clinical application.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

Figure 1

Flowchart illustrating the patient selection process.

Figure 2

Pre-therapy ^{68}Ga -DOTATATE PET/CT of GEP-NETs patients with large and small extrahepatic ^{68}Ga -DOTATATE avid tumor volume. (a) 60-year-old female with Grade 1 small bowel NETs and extensive ^{68}Ga -DOTATATE avid hepatic metastases and peritoneal carcinomatosis (arrow to thickened right anterolateral peritoneum with intense DOTATATE uptake). The patient expired in 2 months. (b) 79-year-old female with Grade 1 small bowel NETs and extensive peritoneal, retroperitoneal and osseous metastases

(arrows to L2 vertebral body sclerotic lesion with intense DOTATATE uptake). The patient expired in 3 months. (c) 71-year-old female with Grade 2 pancreatic NETs and small hepatic metastatic volume and no extrahepatic tumor volume. Patient has progressed at 31 months and alive at 33 months posttherapy. (d) 60-year-old female with Grade 1 pancreatic NETs and extensive 68Ga-DOTATATE avid hepatic metastases but small extrahepatic tumor volume. Patient has progressed at 30 months and alive at 33 months post-therapy.

Figure 3

(a) Kaplan-Meier analysis of PFS in GEP-NETs patients showed that smaller extrahepatic ^{68}Ga -DOTATATE avid tumor volume ($<140\text{ mL}$) is associated with significantly longer PFS (Median PFS 29.0 ± 6.7 months vs 9.0 ± 1.7 months, $P = 0.0001$). (b) This trend in PFS is less prominent when total ^{68}Ga -DOTATATE avid tumor volume ($< 1000\text{ mL}$) is analyzed (Median PFS 24.0 ± 5.4 months vs 10.0 ± 3.4 months, $P = 0.04$). (c) Kaplan-Meier analysis of OS showed that GEP-NETs patients with smaller extrahepatic ^{68}Ga -DOTATATE avid tumor volume ($<150\text{ mL}$) is associated with significantly longer OS (Median OS not reached vs 44.0 ± 12.3 months, $P = 0.002$). (d) This association with OS is not statistically significant for total ^{68}Ga -DOTATATE avid tumor volume ($P = 0.08$).

Figure 4

(a) Kaplan-Meier survival analysis of PFS showed that smaller 68Ga-DOTATATE avid osseous tumor volume (< 50 mL) is associated with longer PFS (Median PFS 22.0 ± 2.4 months vs 7.0 ± 1.1 months, $P = 0.006$). (b) Such trend of PFS is observed in patients with larger 68Ga-DOTATATE avid hepatic tumor volume but less prominent ($P = 0.03$). (c) However, when 68Ga-DOTATATE avid hepatic tumor volume is grouped into low (<500 mL), medium (500-1000mL) and large (> 1000 mL) tumor volumes, no statistically significant difference in PFS is observed ($P = 0.19$). (d) No statistically significant difference is observed in PFS between groups with higher and lower SUVmax values.

Figure 5

GEP-NETs patients were grouped into large and small extrahepatic tumor volumes by visual inspection. Kaplan-Meier survival analysis of PFS showed similar association where smaller extrahepatic tumor volume is associated with longer PFS ($P = 0.005$).

Supplementary Files

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- [FigS1.png](#)