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Surgery enhances the effectiveness of Peptide Receptor Radionuclide Therapy in metastatic Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND

With the advent of Peptide Receptor Radionuclide Therapy (PRRT), the timing and sequence of surgery in the treatment of metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) merits further study. We hypothesized that surgery prior to PRRT might enhance its effectiveness in patients with metastatic GEP-NETs.

METHODS

Eighty-nine patients with metastatic well-differentiated GEP-NETs treated with ¹⁷⁷Lu- DOTATATE PRRT between 2018 and 2023 were included. Fifty-six patients underwent surgery (primary tumor resection and/or liver debulking) prior to PRRT and 33 patients did not. Primary outcome was progression-free survival (PFS) according to RECIST. Pre-treatment DOTATATE PET CT was used to calculate tumor volumes (TV).

RESULTS

The surgery and no-surgery groups were well-matched. Median PFS after PRRT was 15.6 months (IQR 9.1-22.7) in the no-surgery group compared to 26.1 months (IQR 12.7-38.1) in the surgery group ($p=0.04$). On subgroup analysis, median PFS was 18.1 months (IQR 11.9-38.4) in patients who underwent primary tumor resection only versus 26.2 months (IQR 14.0-38.1) in patients who underwent liver debulking ($p=0.04$). TV was lowest in patients who underwent liver debulking (median 146.07mL³) compared to no surgery (median 626.42mL³) ($p = 0.001$). On univariable analysis, TV < 138.8mL³ was associated with longer PFS (HR 2.03 [95% CI 0.95 – 4.34], $p=0.05$), with a median PFS of 38.1 months (IQR 16.9-41.3) versus 17.8 months (IQR 10.8-28.7).

CONCLUSIONS

Surgery may enhance the effectiveness of ^{177}Lu -DOTATATE in the treatment of metastatic well-differentiated GEP-NETs. This positive effect may be due to a lower tumor volume in patients after surgery. Our findings fortify the concept of using surgical debulking to improve systemic therapies such as PRRT.

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