# Supplemental Online Content

Kipnis ST, Hung M, Kumar S, et al. Laboratory, clinical, and survival outcomes associated with peptide receptor radionuclide therapy in patients with gastroenteropancreatic neuroendocrine tumors. *JAMA Netw Open*. 2021;4(3):e212274. doi:10.1001/jamanetworkopen.2021.2274

**eAppendix.** Laboratory Measured Toxic Effects Per Common Terminology Criteria for Adverse Events Version 5.0
**eTable 1.** Univariable Analysis of Factors Associated With Progression Among Patients With Reviewable Imaging After Treatment
**eTable 2.** Univariable Analysis of Factors Associated With Survival After Treatment
**eFigure.** Overall Survival After Treatment

This supplemental material has been provided by the authors to give readers additional information about their work.

**eAppendix.** Laboratory Measured Toxic Effects Per Common Terminology Criteria for Adverse Events Version 5.0[1]

Leukopenia, anemia, and thrombocytopenia were defined as the new development of a WBC count less than 3000/mm$^3$, Hgb less than 10g/dL, and Plt count less than 75,000/mm$^3$ respectively. Nephrotoxicity was defined as the new development of an eGFR less than 60mL/min/1.73m$^2$. Biochemical liver injury was defined as the new development of a total bilirubin greater than 1.5x the upper limit of normal, AST greater than 3x the upper limit of normal, or ALT greater than 3x the upper limit of normal.

Grade 3/4 toxicities were defined as WBC count less than 2000/mm$^3$, Hgb less than 8g/dL, and Plt count less than 50,000/mm$^3$ respectively. Grade 3/4 nephrotoxicity was defined as the new development of an eGFR less than 30mL/min/1.73m$^2$. Grade 3/4 biochemical liver injury was defined as the new development of a total bilirubin greater than 3x the upper limit of normal, AST greater than 5x the upper limit of normal, or ALT greater than 5x the upper limit of normal.
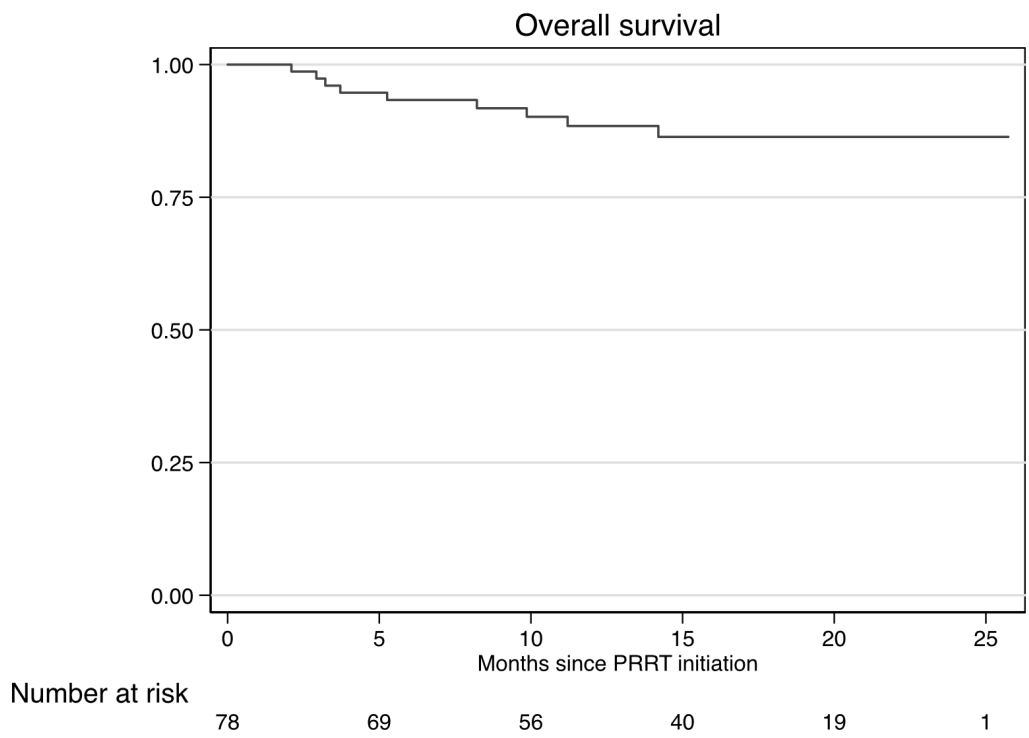
**eTable 1.** Univariable Analysis of Factors Associated With Progression Among Patients With Reviewable Imaging After Treatment

| | HR (95% CI) | P-value |
|---|---|---|
| Age at diagnosis (years), median (IQR) | 1.01 (0.97-1.05) | 0.58 |
| Age at first PRRT (years), median (IQR) | 0.99 (0.95-1.03) | 0.68 |
| Male sex | 0.82 (0.37-1.82) | 0.63 |
| NET primary location | | |
|    Pancreas | REFERENCE | |
|    Small bowel | 0.21 (0.07-0.59) | **<0.01** |
|    Other/unknown | 0.58 (0.24-1.43) | 0.24 |
| Grade of NET | | |
|    1 | REFERENCE | |
|    2 | 1.22 (0.44-3.36) | 0.70 |
|    3 | 3.07 (0.86-11.00) | 0.09 |
| Systemic therapy prior to PRRT | 1.09 (0.49-2.44) | 0.83 |
| Liver-directed therapy prior to PRRT | 0.71 (0.32-1.58) | 0.40 |
|    Hepatic resection | 1.02 (0.42-2.45) | 0.97 |
|    Radiofrequency ablation | 0.73 (0.10-5.44) | 0.76 |
|    Bland embolization | 0.76 (0.22-2.55) | 0.65 |
|    TACE | 0.70 (0.24-2.07) | 0.52 |
|    TARE | 0.91 (0.31-2.67) | 0.87 |
| Prior resection of primary | 0.76 (0.32-1.79) | 0.53 |

**eTable 2:** Univariable Analysis of Factors Associated With Survival After Treatment

| | HR (95% CI) | P-value |
|---|---|---|
| Age at diagnosis (years), median (IQR) | 1.08 (1.01-1.16) | **0.02** |
| Age at first PRRT (years), median (IQR) | 1.07 (0.99-1.15) | 0.10 |
| Male sex | 1.96 (0.49-7.85) | 0.34 |
| NET primary location | | |
|    Pancreas | REFERENCE | |
|    Small bowel | 1.25 (0.11-13.78) | 0.86 |
|    Other/unknown | 6.39 (0.77-53.19) | 0.09 |
| Grade of NET | | |
|    1 | REFERENCE | |
|    2 | 1.47 (0.27-8.01) | 0.66 |
|    3 | 1.58 (0.14-17.43) | 0.71 |
| Systemic therapy prior to PRRT | + | 1.00 |
| Liver-directed therapy prior to PRRT | 0.49 (0.13-1.82) | 0.28 |
|    Hepatic resection | 0.33 (0.04-2.67) | 0.30 |
|    Radiofrequency ablation | 1.38 (0.17-11.04) | 0.76 |
|    Bland embolization | 1.58 (0.33-7.64) | 0.57 |
|    TACE | 0.44 (0.05-3.51) | 0.44 |
|    TARE | 0.64 (0.08-5.10) | 0.67 |
| Prior resection of primary | 0.48 (0.13-1.79) | 0.27 |

**eFigure.** Overall Survival After Treatment
OS for the entire cohort of individuals with metastatic NETs who underwent PRRT.



Overall survival

Number at risk

| 78 | 69 | 56 | 40 | 19 | 1 |

**Supplemental Content References**

1. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

November 27, 2017. Accessed October 12, 2020.

https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm - ctc_50