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¹⁷⁷Lu-DOTATATE/DOTATOC

Re-Treatment in Patients with Progressive Neuroendocrine Tumours: A Systematic Review and Meta-Analysis



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BACKGROUND: Initial peptide receptor radionuclide therapy (PRRT) with ¹⁷⁷Lu-DOTATATE (LUTATHERA[®]) is approved in adults with somatostatin receptor-positive gastroenteropancreatic NETs. This review and meta-analysis examined published evidence of the efficacy and safety of re-treating patients with advanced NETs with ¹⁷⁷Lu-DOTATATE/DOTATOC.

METHODS: Embase, MEDLINE, MEDLINE In-Process, and Cochrane CENTRAL were searched to identify all published evidence related to clinical efficacy and safety of ¹⁷⁷Lu-DOTATATE/DOTATOC in PRRT-pretreated adults with advanced NETs. The feasibility of combining studies to calculate pooled efficacy (progression-free survival [PFS], overall survival [OS], disease control rate [DCR]) from time of re-treatment was assessed. Data were pooled using medians and variance for time-to-event outcomes and inverse-variance weighted proportions (Freeman-Tukey method) for binary outcomes.

RESULTS: Of 567 studies screened for eligibility, 8 reported re-treatment efficacy outcomes and were included. In random-effects meta-analyses, median PFS (n=5 studies [272 patients]) was estimated as 12.26 months (95% CI, 9.06-15.47) with moderate heterogeneity across studies ($I^2=42.6\%$), and mean OS (n=2 [200 patients]) was estimated as 38.44 months (95% CI, 14.14-62.74) with extreme heterogeneity ($I^2=92.9\%$).

Pooled DCR by RECIST v1.1 (n=3 [215 patients]) and SWOG (n=2 [66 patients]) criteria from random-effects meta-analyses were 75% (95% CI, 69-81%) and 47% (95% CI, 35-59%), respectively, with no evidence for heterogeneity ($I^2=0\%$). The safety profile of PRRT re-treatment (n=5 [296 patients]) was similar to initial PRRT treatment, with grade 3-4 adverse events occurring in 7% (95% CI, 3-11%) of patients. No grade 3-4 renal toxicities were reported. Incidences of myelodysplastic syndrome and acute myeloid leukemia ($\approx 1\%$) were low.

CONCLUSION: The safety profile of re-treatment with ^{177}Lu -DOTATATE/DOTATOC was similar to that of initial treatment. Following initial ^{177}Lu -DOTATATE/DOTATOC, re-treatment provided an encouraging median PFS duration and DCR in patients with NETs, though heterogeneity compromised OS meta-analysis.

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