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Efficacy and safety of [177Lu]Lu-edotreotide ([177Lu]Lu-DOTATOC) for the treatment of neuroendocrine tumors (NETs) – a systematic literature review (SLR) and meta-analysis

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BACKGROUND

[^{177}Lu]Lu-edotreotide represents a promising radiopharmaceutical therapy (RPT) currently undergoing clinical evaluation for its efficacy in the management of patients with advanced NETs. No meta-analysis of data has previously been published for [^{177}Lu]Lu-edotreotide in this clinical setting.

METHODS

PubMed, EMBASE, Cochrane databases, and abstracts from select congresses were searched for eligible [^{177}Lu]Lu-edotreotide studies (PROSPERO 2024 CRD42024518028). Meta-analyses were performed using fixed and random-effects models. The primary outcome was the objective response rate (ORR; complete + partial response) in the subgroup of patients with gastroenteropancreatic NETs (GEP-NETs) and in those with any NETs, irrespective of origin (All-NETs). Secondary outcomes included disease control rate (DCR; best overall response of complete response + partial response + stable disease), median progression-free survival (mPFS), and median overall survival (mOS). Safety/tolerability data for [^{177}Lu]Lu-edotreotide were reviewed but not analyzed. Unpublished/updated data were requested from the authors where needed, to permit additional analyses.

RESULTS

Of 591 unique publications identified in the searches, eight studies were eligible for inclusion, all in the advanced disease setting (5/8 included patients with progressive NETs). Updated data were included from 4/8 studies (maximum n=294 GEP-NETs; n=489 All-NETs). Most patients had grade 1/2 NETs (grade 1: 11%–63%; 2: 30%–79%; 3: 4%–11%). The response was assessed using RECIST-based criteria in 4/8 studies. There was high heterogeneity (I^2 >70%) across meta-analysis outcomes/patient

populations, therefore, results from the more conservative random-effects model were prioritized. Patients with GEP-NETs had better RPT efficacy outcomes than those with All-NETs (Table). Safety/tolerability data were inconsistently reported, but grade 3/4 hematological, renal and hepatic toxicities were rarely noted during [^{177}Lu]Lu-edotreotide treatment. No secondary malignancies were reported in patients receiving RPT with [^{177}Lu]Lu-edotreotide alone.

Meta-analysis efficacy results (random-effects model)

	GEP-NETs	All-NETs
ORR, % (95% CI)	34 (17–54) [n=222]	19 (8–32) [n=423]
DCR, % (95% CI)	78 (60–92) [n=222]	57 (33–79) [n=423]
mPFS, months (95% CI)	24.9 (17.6–32.2) [n=294]	18.6 (12.5–24.8) [n=267]
mOS, months (95% CI)	44.8 (36.8–52.8) [n=256]	39.1 (25.1–53.0) [n=408]

CI = confidence interval; n = number of patients in analysis

CONCLUSIONS

Overall, these results show favorable efficacy for [^{177}Lu]Lu-edotreotide in patients with advanced NETs, especially in those with GEP-NETs. Response and PFS outcomes were encouraging in relation to recent phase 3 [^{177}Lu]Lu-edotreotide data from COMPETE. The safety/tolerability profile of [^{177}Lu]Lu-edotreotide also appears to be good and in line with the findings in COMPETE.

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