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The Role of Somatostatin Analogue Maintenance Therapy in Refractory Metastatic Neuroendocrine Tumors (NETs): Comparative Analysis

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BACKGROUND

Somatostatin analogues (SSAs) are the standard of care first line therapy for metastatic well-differentiated neuroendocrine tumors (NETs). They are approved for both alleviating hormone-related symptoms for functional tumors and inhibiting tumor growth. Their anti-proliferative benefit in the refractory setting is debatable due to lack of supportive literature. This systematic review compared efficacy of targeted therapies (Everolimus, Sunitinib, Surufatinib, Lenvatinib, Nintedanib, Pazopanib, Axitinib) with and without SSAs in refractory metastatic NETs.

METHODS

15 prospective clinical trials published from 2008 to 2020 (8 used targeted therapy alone, 5 used targeted therapies with SSA and 2 used both) were included in final analysis. In a meta-analytic approach, proportions of a characteristic by therapy subgroup and associated p-value for the subgroup comparison were calculated from random effects models. Similar methods for incidence rates were used to evaluate incidence of progression.

RESULTS

2,495 metastatic well-differentiated NET patients were identified; 1,824 were categorized into group A [patients who received targeted therapy alone 59.5% (n =1,087)] or group B [patients who received combined targeted therapies with SSAs 40.4% (n =737)] and the rest of the patients in these trials received placebo. The median age was 58 years old, and 52.9% were males while 47.1% were females. Primary lesions were pancreas (42%), gastrointestinal (32%), lung and thymus (16%), others/unknown (10%).

Pathological grades were G1 (45%), G2 (52%), G3 (3%). There were no significant differences in terms of objective response rate (ORR) between group A 0.096 (95% CI 0.057-0.156), and group B 0.098 (95% CI 0.047-0.192), (P= 0.9587). In addition, there was no significant difference in the incidence of progression between the two groups [group A: 0.0646 per person year, (95% CI 0.055-0.074) vs group B: 0.0561 per person year, (95% CI 0.039-0.080), (P= 0.473)]. Grade 3 and 4 side effects (fatigue, nausea and transaminitis) were higher in SSA combination therapy, but sample size was limited due to heterogeneous reporting and low incidence rates.

CONCLUSIONS

Addition of maintenance SSAs to targeted therapies was not associated with significant benefit in tumor control in patients with refractory metastatic NETs. These results need to be validated in prospective randomized controlled trials designed to include both survival benefit and associated financial toxicity.

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