

Escalated Dose Somatostatin Analogues (SSA) in Management of NETs: A Systematic Review

David L Chan¹; Diego Ferone²; Manuela Albertelli²; Simron Singh¹

¹Odette Cancer Centre; ²IRCCS AOU San Martino-IST, University of Genoa, Italy

Background: SSAs are effective in controlling NET symptoms and more recently have been shown to have anti-proliferative properties. PROMID and CLARINET have established “standard” doses of octreotide and lanreotide, but dose escalation is often employed both for symptom relief and tumor control.

Methods: We searched MEDLINE, EMBASE, Cochrane CENTRAL and abstracts of major conferences. Studies investigating patients treated with doses of octreotide higher than 30mg/28d or lanreotide higher than 120mg/28d were eligible for inclusion. Data extracted included patient population, interventions and prior SSA use. The primary endpoint was disease control rate; secondary endpoints included response rate, symptom control, biochemical response, progression-free survival and toxicity.

Results: 22 studies (13 prospective; 1019 patients) were identified from 609 search results. Of the 13 studies that mandated prior treatment, the reasons for dose escalation were tumor progression (5), symptoms (3), either (2) and not listed (3). SSAs used were octreotide LAR (11), lanreotide ATG (1), short-acting octreotide (3), short-acting lanreotide (6), and mixtures (2). Significant heterogeneity existed in dosing schedules as well as reporting of efficacy data.

Disease control rate ranged from 40-100% (pooled rate 327/515) with response rates from 0-42% (pooled rate 28/515). Dose escalation was associated with improvement in carcinoid symptoms in at least 50% of patients. Biochemical response was variably defined but reported rates ranged from 33% to 100% (pooled rate 56/79). PFS ranged from 7 months to 32 months. Dose escalation was generally well tolerated with side effect profile and frequency comparable to normal dose SSA.

Conclusion: Conclusion: Escalated dose SSA is well tolerated and results in significant rates of disease control and symptomatic improvement. Compared to a prior systematic review (Broder WJG 2015), this review adds review of lanreotide, includes 6 new studies with 600 additional patients, and restricts inclusion to clinical studies. Prospective randomized trials of escalated SSA therapy are warranted.