A Systematic Literature Review on the Efficacy and Safety of Octreotide Long-Acting Repeatable Used at Higher than FDA-Approved Doses and/or Frequencies for Treatment of Neuroendocrine Tumors

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Background: Octreotide-LAR is FDA approved for alleviating severe diarrhea/flushing associated with metastatic carcinoid tumors at doses ≤30mg every 4 weeks. In clinical practice, octreotide long-acting repeatable (LAR) is sometimes prescribed at above-label doses, but evidence for this practice has not been systematically assessed. We reviewed published literature on efficacy and safety of octreotide-LAR at doses >30mg/month for treatment of neuroendocrine tumors (NETs).

Methods: PubMed and Cochrane Library from 1998-2012, 5 conferences (ASCO, ENDO, ENETS, ESMO, NANETS) from 2000-2013, and bibliographies of included articles were searched using MeSH and keyterms—including “neuroendocrine tumors,” “carcinoid tumor,” “carcinoma, neuroendocrine,” and “octreotide.” Title/abstract/full length article review was conducted by 2 reviewers. Included studies reported data on efficacy and safety of ≥30mg/month octreotide-LAR for NETs in human subjects, published in any language.

Results: Of 1086 identified publications, 238 underwent full-text review (20 following translation into English), and 18 were included (weighted-kappa: 0.94). Studies varied in design, patients, octreotide-LAR regimens, and definition of outcomes. Efficacy was reported in 11 studies describing 260 subjects with doses ranging from 40mg/month or 30mg/3 weeks up to 120mg/month. Although studies lacked quantitative measurements of symptom severity and formal quality-of-life analysis, higher doses were used to control symptoms and tumor progression in 12 studies. Expert opinion in 8 studies supported dose escalation up to 60mg/month for symptom control and suggested increased doses may be effective for tumor progression. Safety was reported in 8 studies. Five supported the tolerability of higher dose octreotide-LAR and 3 did not report results by dose, although study sample sizes may have been too small to identify rare events.

Conclusions: The use of above-label doses of octreotide-LAR for symptom and tumor control of NETs has been described in several studies within the published literature.