19 studies (12 prospective, 7 retrospective) were identified. Doses varied from 40mg/28d to 160mg/14d for octreotide, and response rates ranged from 0-14%; DCR from 30-100%. In methods, the aims were to perform a systematic review regarding escalated dose SSAs in the treatment of NETs. 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. Dose escalation is often employed both for symptom relief and tumour control, but with little trial evidence to support this approach.

**Aims**

To perform a systematic review regarding escalated dose SSA in the treatment of GEPNETs.

**Methods**

- MEDLINE, EMBASE, Cochrane CENTRAL and abstracts of major conferences underwent dual independent review.
- Eligible studies investigated >5 patients treated with doses of octreotide higher than 30mg/28d or lanreotide higher than 120mg/28d.
- 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.
- Qualitative synthesis was chosen over meta-analysis given the anticipated clinical heterogeneity in identified trials.

**Results**

- 19 studies (12 prospective, 7 retrospective) were identified with a total of 981 patients. (Fig.1)
- Doses varied from 40mg/28d to 160mg/14d for octreotide, and from 180mg/28d to 420mg/28d (15mg/d) for lanreotide.
- Response rates ranged from 0-14%; DCR from 30-100%. In general, rates of biochemical and symptomatic response exceeded 50%.

**Discussion**

- Significant heterogeneity was present – in terms of SSAs used, dosages employed, site of primary and trial design.
- No randomized trials comparing escalated dose SSA to standard dose SSA were identified. Although dose escalation is commonly done, there is relatively little information on clinical outcomes from this strategy.
- No pharmacokinetic data existed in the above trials, although significant peak-to-trough variability was noted for both octreotide and lanreotide (Woltering Pancreas 2005, Astruc J Clin Pharmacol 2005).

**Conclusions**

- Dose escalation of SSAs has been trialled in both prospective and retrospective settings, but no randomized trials exist comparing it with standard dose SSA.
- Trials formally investigating the use of increased dose SSAs are warranted to optimize their place in the NET treatment paradigm.