

 OBESITY

## Repurposed agent shows weight-loss potential

A Phase II trial of tesofensine, an inhibitor of the presynaptic uptake of noradrenaline, dopamine and serotonin, suggests that it might induce double the weight loss in obese patients compared with currently used pharmacotherapies.

Tesofensine was initially under investigation in Alzheimer's disease and Parkinson's disease to improve cognitive function, but although it showed limited efficacy in this respect,

it also induced unintended weight loss. So, to further assess its potential as an anti-obesity drug, Astrup *et al.* undertook a randomized, double-blind, placebo-controlled, parallel group study in which 203 obese patients were assigned 0.25 mg, 0.5 mg or 1.0 mg of tesofensine or placebo once daily for 24 weeks. The primary efficacy end point was percentage change in body weight.

The results of the trial, published in *The Lancet*, show that all doses of tesofensine produced a significantly greater mean weight loss than placebo and diet. For example, patients receiving the 0.5 mg dose showed a 9.2% mean weight reduction (corresponding to 9.1 kg) above that of placebo, and the proportion of patients who achieved more than 5 kg or more weight loss was 87%, compared with 29% in the placebo group. Weight loss was mainly due to loss of body fat.

Overall, the most common adverse events experienced by those on tesofensine included dry

mouth, nausea, insomnia, abdominal pain, constipation and diarrhoea. The 1.0 mg dose produced slightly greater weight loss (10.6%) than the 0.5 mg dose, but was associated with more adverse events and a higher level of treatment discontinuation. Heart rate also increased in patients receiving tesofensine, which could be an important safety issue for obese patients with increased cardiovascular risks.

In analogous trials of other anti-obesity drugs, net weight losses of 2.9 kg, 4.2 kg and 4.7 kg have been achieved with orlistat, sibutramine and rimonabant, respectively, over the same time period. So, the authors suggest that tesofensine 0.5 mg once daily for 6 months has the potential to induce weight loss twice that induced by currently approved drugs, and Phase III trials are anticipated to begin next year.

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**ORIGINAL RESEARCH PAPER** Astrup, A. *et al.* Effect of tesofensine on bodyweight loss, body composition, and quality of life in obese patients: a randomised, double-blind, placebo-controlled trial. *Lancet* 22 Oct 2008 (doi:10.1016/S0140-6736(08)61525-1)



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