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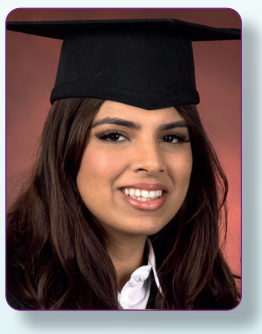

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Efficacy and Safety of Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss Among Adults Without Diabetes : A Systematic Review of Randomized Controlled Trials

Areesha Moiz, Kristian B. Filion, Helia Toutounchi, Michael A. Tsoukas, Oriana H.Y. Yu, Tricia M. Peters, and Mark J. Eisenberg.

Our systematic review was designed to assess the efficacy and safety of GLP-1 Ras, which includes Saxenda® and WeGovy® for example, and co-agonists for weight loss in otherwise healthy adults with overweight or obesity and without diabetes.

Previous systematic reviews and meta-analyses of randomized controlled trials (RCTs) have examined the efficacy and safety of GLP-1 RAs for weight loss in people with overweight or obesity, both with diabetes and without diabetes. However, these studies included patients with co-existing conditions, such as metabolic disorders or cardiovascular disease. Our systematic review differs from these previous studies in that we restricted inclusion to otherwise healthy adults with overweight or obesity.

Our search identified 26 randomized controlled trials (RCTs) of 12 agents, including 3 which are FDA-approved and commercially available for weight management (liraglutide, semaglutide, and tirzepatide) and 9 agents in the pre-market stage. Of the 3 FDA-approved agents, once-daily liraglutide led to weight loss of up to 6%, once-weekly semaglutide of up to 14%, and once-weekly tirzepatide of up to 18% when compared to placebo. The premarket agents identified by our search also showed promising weight loss and cardioprotective effects. A phase 2 RCT assessing retatrutide, a triple agonist, showed the greatest placebo-subtracted weight loss of around 22%. The use of all GLP-1 RAs or co-agonists led to decreased BMI, waist circumference, SBP, and DBP. Similar safety profiles were observed across agents. The rate of GI AEs was higher in the GLP-1 RA groups than the placebo groups. However, these events were described as transient, related to dose escalation, and mild to moderate in severity. The rate of AEs requiring treatment discontinuation, SAEs, and death was low across all RCTs.

However, these trials did not compare therapies head-to-head, precluding conclusions about their comparative efficacy. Our results support the use of GLP-1 RAs and co-agonists for the treatment of overweight or obesity among patients without diabetes.

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