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Summary

Gut hormone co-agonists for the treatment of metabolic syndrome: From bench to bedside

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This presentation traces the 20-30 year development of gut hormone-based obesity therapies from early glucagon/GLP-1 dual agonists through current GIP/GLP-1 dual agonists to investigational triple agonists, with the speaker reporting that these drugs achieve progressive weight loss but require ongoing treatment.

KEY POINTS

- The speaker reported that dual GIP/GLP-1 agonists such as tirzepatide produce 22-23% average body weight loss in human obesity and normalize HbA1c in more than half of type 2 diabetes patients.
- Triple receptor agonists targeting glucagon, GLP-1, and GIP receptors showed 24% weight loss in 48 weeks in phase 2 trials as stated by the speaker, with phase 3 data expected next year and potential approval within two years.
- The speaker stated that dual agonists provide improved benefits over mono-agonists without proportionally increased gastrointestinal side effects because GIP appears to suppress GLP-1-related nausea and emesis.
- Preclinical work identified GABAergic GIP neurons in the hindbrain as the master switch for the additional benefits of dual agonism according to the speaker.
- The speaker emphasized these are management drugs not cures, with weight regain occurring after discontinuation similar to blood pressure medications, and ongoing treatment is required to maintain metabolic benefits.
- The speaker noted speculative signals for benefits beyond obesity including cardiovascular effects, addiction reduction particularly for alcohol, and possible effects on neurodegenerative diseases, though mechanisms remain unclear.

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