Tirzepatide Frequently Asked Questions

Dosage and Dose Escalation in Clinical Trials

How was tirzepatide administered and what doses were used in the SURPASS clinical trials?

- Tirzepatide was administered once weekly by subcutaneous injection. As detailed below, all participants were initiated on the 2.5-mg strength and dose-escalated to the randomized doses of 5 mg, 10 mg, or 15 mg.

At what dose was tirzepatide initiated and how was the dose escalated?

- All participants in the tirzepatide treatment arms initiated tirzepatide at a dose of 2.5 mg once-weekly. The dose was then escalated in 2.5-mg increments every 4 weeks until the randomized dose of 5 mg, 10 mg or 15 mg was reached. Therefore, the 5-mg, 10-mg and 15-mg doses were reached in 4 weeks, 12 weeks and 20 weeks, respectively.

Using Tirzepatide with other Treatments for T2D

Was tirzepatide used as an adjunct therapy only, or was it used as a monotherapy?

- The SURPASS phase 3 global clinical development program assessed tirzepatide as an add-on to various standard-of-care medications including the selective GLP-1 RA once-weekly injectable semaglutide 1 mg, insulin glargine, and insulin degludec for T2D. Clinical trial results support its use as the only pharmacological therapy (monotherapy) and also as an adjunct to other antidiabetic medications, including insulin.
- Tirzepatide was assessed as monotherapy (versus placebo) in patients treated at baseline with diet and exercise only (SURPASS 1). In other trials, tirzepatide was assessed versus active comparators or placebo in patients treated at baseline with oral agents (SURPASS 2, 3, 4) as well as basal insulin (SURPASS 5).

In the clinical trials assessing patients taking metformin, was metformin discontinued or was the dose changed?

- In clinical trials assessing tirzepatide in patients with T2D using metformin, metformin was continued and its dose was not changed.

Measuring Success

Was A1c the primary measure of success for tirzepatide?

- Yes, the change in HbA1c was the primary endpoint for each of the SURPASS clinical trials. In each study, tirzepatide achieved its primary and key secondary endpoints (including change in body weight) for the and delivered consistent safety and efficacy with sustained A1C reduction and progressive weight loss among people with T2D.

How soon after beginning tirzepatide was improvement in A1c seen?

- In the tirzepatide Phase 3 clinical trials, improvement in glucose as measured by A1c was seen as soon as 4 weeks after initiation of tirzepatide and continued to improve thereafter.

Weight Change with Tirzepatide

Does weight loss due to tirzepatide vary if the patient is also on metformin or insulin?

- There is no head-to-head study assessing the effect of tirzepatide on body weight loss in patients with T2D treated with metformin versus patients treated with insulin. In clinical trials assessing tirzepatide as add-on therapy to metformin or as an add-on to basal insulin, tirzepatide at 5 mg, 10 mg, and 15 mg resulted in significant weight reduction from baseline at 40 and 52 weeks.

Did weight loss due to tirzepatide eventually taper off?

- In the clinical trials assessing patients with T2D, weight loss at the highest dose of tirzepatide (15 mg) plateaued around 52 weeks (1 year).

How soon after discontinuing tirzepatide was weight regained?

- This has not been assessed in clinical trials, and so it is not currently known.

Effects on Dyslipidemia

Does tirzepatide improve dyslipidemia in patients?

- In clinical trials, tirzepatide has been shown to improve patients' lipid profiles, including a reduction in triglyceride levels and an increase in HDL cholesterol levels.

Is there any comparison between GLP-1 RAs and tirzepatide in improving dyslipidemia?

- Yes. In the SURPASS-2 study, assessing tirzepatide (5 mg, 10 mg, and 15 mg once weekly) versus semaglutide (1 mg once weekly) in patients with T2D treated with metformin, tirzepatide-treated patients had lower triglyceride and higher HDL cholesterol levels after 40 weeks of treatment than did semaglutide-treated patients.

Risk of Hypoglycemia

What are the risks of hypoglycemia with tirzepatide?

- Based on the mechanism of action of tirzepatide, the risk of clinically significant hypoglycemia is very low when used as monotherapy or in conjunction with another antihyperglycemic agent with a low risk of hypoglyemia such as metformin or an SGLT2 inhibitor.

Adverse Events

What were the most common adverse events that patients on tirzepatide encountered?

- As with selective GLP-1RAs (eg, dulaglutide and semaglutide), the most common adverse events observed in clinical trials with tirzepatide were gastrointestinal in nature. These included nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain. In a pooled analysis of two placebo-controlled trials (SURPASS-1 and SURPASS-5), the incidence of gastrointestinal side effects in tirzepatide-treated patients was higher than that in patients receiving placebo and tended to increase with increasing tirzepatide dose.

Do gastrointestinal side effects that occur with tirzepatide dissipate on their own?

- In clinical trials, if patients taking tirzepatide experienced gastrointestinal side effects, they tended to occur early in the course of therapy (during dose escalation), be mild or moderate in severity, and resolve over time. Relatively few patients had to stop tirzepatide because of gastrointestinal side effects. For example, in a pooled analysis of placebo-controlled clinical trials, discontinuation of treatment due to gastrointestinal side effects occurred in 3.0%, 5.4%, 6.6%, and 0.4% in patients treated with tirzepatide 5 mg, 10 mg, 15 mg, and placebo, respectively.

Precautions

Was tirzepatide assessed in patients with retinopathy?

- Tirzepatide was not studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema.

For additional detail see:

- Rosenstock J, et al. Lancet. 2021;398:143-155.
- Frías JP, et al. N Engl J Med. 2021;385:503-515.
- Ludvik B, et al. Lancet. 2021;398:583-598.
- Del Prato S, et al. Lancet. 2021;398:1811-1824.
- Dahl D, et al. J Amer Med Assoc. 2022;327:534-545.