Clinical Trials Update

Tirzepatide Trial Demonstrates Substantial Weight Loss
A trial reported in the New England Journal of Medicine evaluated the drug tirzepatide for treatment of obesity or overweight among adults without diabetes. Participants experienced substantial and sustained weight loss with a weekly injection of the novel glucose-dependent insulino-tropic polypeptide and glucagon-like peptide-1 receptor agonist, which is approved for type 2 diabetes.

Study participants were randomly assigned to receive tirzepatide or placebo once a week for 72 weeks, including a 20-week dose-escalation period. All received counseling to eat 500 fewer calories per day and to exercise for at least 150 minutes per week.

The 2,539 participants’ average body weight was 104.8 kg and their average body mass index was 38 at the start of the trial. By week 72, participants in the intervention group lost an average 15% of their body weight with a 5-mg dose, 19.5% with a 10-mg dose, and 20.9% with a 15-mg dose, compared with 3.1% average weight loss in the placebo group.

In the intervention group, 85% to 91% of participants reduced their weight by 5% or more compared with 35% in the placebo group. Half of the 10-mg tirzepatide group and 57% of the 15-mg group reduced their body weight by 20% or more. The intervention group also had improved cardiovascular and metabolic measures, and the adverse events they experienced were mainly mild to moderate gastrointestinal issues during dose escalation.

Evusheld Reduces COVID-19 Disease Severity Among Unvaccinated Adults
Tixagevimab plus cilgavimab, a SARS-CoV-2-neutralizing monoclonal antibody combination marketed as Evusheld, protected nonhospitalized individuals with mild to moderate COVID-19 symptoms from progressing to severe COVID-19 or death in a clinical trial. The study, published in The Lancet Respiratory Medicine, is the first to evaluate the intramuscular injection for outpatient treatment; other anti-SARS-CoV-2 monoclonal antibodies must be administered intravenously or subcutaneously.

The international TACKLE trial randomly assigned 910 adults with mild or moderate COVID-19 symptoms to receive a single 300-mg dose of tixagevimab plus a 300-mg dose of cilgavimab or placebo within 7 days of symptom onset. The trial was conducted between January and July 2021, prior to widespread COVID-19 vaccination, and enrolled only unvaccinated people. About 90% of participants were at high risk of severe COVID-19 due to age or comorbidities.

Severe COVID-19 or death occurred in 4% of the 407 participants in the tixagevimab-cilgavimab group, which reported 3 deaths, compared with 9% of 415 participants in the placebo group, which reported 6 deaths. Adverse events were mostly mild or moderate and were more frequent in the placebo group.

Evusheld received US Food and Drug Administration (FDA) Emergency Use Authorization for COVID-19 prevention in December 2021. AstraZeneca is in discussions with the FDA about a new indication for COVID-19 treatment, a spokesperson for the drug manufacturer wrote in an email.

Durable IBS Response From Fecal Microbiota Transplant
Years after receiving a fecal microbiota transplant (FMT) as part of a clinical trial, individuals with irritable bowel syndrome (IBS) continued to have fewer abdominal symptoms and fatigue and a better quality of life than they did before the procedure.

The follow-up study published in Gastroenterology included 125 patients who had been randomly assigned to receive either 30 g or 60 g of feces from the same donor or a placebo transplant containing their own feces, both treatments administered to the duodenum.

Three years after FMT, the response rate was 64.9% in the 30-g group, 71.8% in the 60-g group, and 27% in the placebo group, with no long-term adverse events. A fecal composition analysis found that microbiota dysbiosis decreased in the active treatment groups.

Patients with overweight or obesity who took tirzepatide in a clinical trial lost up to 21% of their body weight compared with an average 3.1% weight loss in the placebo group.

Emergency Contraception Caution for Women With Obesity
Studies have shown that women with obesity have more than a 4-fold greater risk of pregnancy using emergency contraception containing levonorgestrel at the standard dose than do women with normal weight. Yet simply doubling the dose doesn’t improve ovulation inhibition among women with obesity, according to a recent trial.

The study enrolled 70 women with a body mass index higher than 30 and body weight of at least 176 lb (79.8 kg). Participants were monitored until a dominant ovarian follicle was apparent on ultrasound. After receiving a negative pregnancy test result, the women were randomly assigned to a 1.5-mg or 3-mg dose of levonorgestrel and monitored for evidence the follicle had ruptured.

The higher levonorgestrel dose did not reduce the risk or timing of ovulation among women who received it at an optimal time in their cycles. Until studies provide additional insights, the authors wrote in Obstetrics & Gynecology, “use of ulipristal acetate for emergency contraception in individuals with obesity who desire an oral agent seems likely to provide the best outcomes.” – Anita Slomski

Note: Source references are available through embedded hyperlinks in the article text online.