Golimumab preserves beta-cell function in children and young adults with Type 1 diabetes

June 16 2020, by Ellen Goldbaum

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In research led by a University at Buffalo pediatric endocrinologist, a

drug called golimumab showed that it preserved beta-cell function in children and young adults with newly diagnosed Type 1 diabetes, according to findings from a Phase 2 study.

The study also demonstrated that golimumab, an anti-tumor-necrosis-factor (TNF) therapy, reduced the amount of injected insulin required by children and young adults with newly diagnosed Type 1 diabetes by preserving their ability to produce insulin on their own, called endogenous insulin. The World Without Disease Accelerator, through Janssen Research & Development, LLC, funded the study.

Golimumab, marketed as Simponi, is currently used in the treatment of rheumatoid arthritis, ulcerative colitis and other autoimmune conditions, however it is not approved by the U.S. Food and Drug Administration for the treatment of Type 1 diabetes.

The findings were presented on June 13 at the annual meeting of the American Diabetes Association by the lead investigator, Teresa Quattrin, MD, UB Distinguished Professor in the Department of Pediatrics, senior associate dean for research integration in the Jacobs School of Medicine and Biomedical Sciences at UB and attending pediatric endocrinologist at the Diabetes Center at UBMD Pediatrics and John R. Oishei Children's Hospital.

"This study shows that golimumab is a potential disease-modifying agent for newly diagnosed patients with Type 1 diabetes," said Quattrin. "The main goal of the study was to see if golimumab could preserve beta-cell function in these newly diagnosed patients."

Measuring how well the pancreas is working

This was assessed by measuring the amount of C-peptide in patients' blood during a four-hour mixed meal tolerance test. Because C-peptide

reflects only insulin made by the body and not injected insulin, C-peptide levels reveal how well the pancreas is producing insulin.

Patients treated with golimumab had a higher C-peptide level at week 52 compared to placebo. "This was statistically significant, thus the study met its primary goal," Quattrin said, "in fact, 41.1% of participants receiving golimubab had an increase or less than 5% decrease in C-peptide compared to only 10.7% in the placebo group."

Good control with less insulin

Nearly 43% of those who received golimumab were in partial diabetes remission (also known as the honeymoon phase) versus 7.1% of those receiving placebo. The definition of partial remission was based on insulin dose and blood sugar control levels as indicated by hemoglobin A1C, a measurement of average blood sugar levels over three months.

Quattrin explained that a child with Type 1 diabetes requires about 1 unit of insulin per kilogram of body weight per day. That means that a child weighing about 65 pounds typically requires about 30 units of injected insulin per day once they are out of the partial remission period, about 3-6 months after diagnosis.

"In this study, both golimumab and placebo groups achieved good blood sugar control, but patients treated with golimumab achieved it with less insulin," said Quattrin. "During the 52 weeks, insulin dose increased only slightly for those on golimumab, 0.07 units per kilogram per day, versus 0.24 units per kilogram per day for those on placebo study. Moreover, in a post-hoc analysis, an analysis conducted after the conclusion of the clinical trial, those who were younger than 18 years had 36% fewer episodes where blood sugar was less than 54 mg per deciliter, designated by the American Diabetes Association as level 2 hypoglycemia," Quattrin said.

This is important clinically because low blood sugar reactions are dangerous and can even be fatal if untreated. Low blood sugars require immediate attention, often causing the child to be removed from class or recreation activities compromising quality of life.

The drug is self-administered as a subcutaneous injection every 2 weeks. No serious side effects related to the study drug, such as serious infections, were reported.

The randomized, controlled clinical trial was conducted at 27 centers throughout the U.S., including at the Diabetes Center at UBMD Pediatrics and Oishei Children's Hospital in Buffalo. It involved 84 patients, aged 6 to 21 years, with two-thirds receiving golimumab and one-third receiving placebo starting within 100 days from diagnosis.

Throughout three decades as a leading researcher in pediatric endocrinology, Quattrin has been interested in finding ways to preserve beta-cell function in newly diagnosed patients with Type 1 diabetes.

The current study took place on the basis of positive findings in animal models, as well as Quattrin's work with patients treated at the Diabetes Center at UBMD Pediatrics and Oishei Children's Hospital. It confirms results published by her team in 2009 where in a randomized pilot study 10 patients received another TNF inhibitor and 8 received placebo starting within 28 days from diagnosis. The results of this small proof of concept study strongly suggested that this class of drugs might be able to preserve beta-cell function in newly diagnosed patients with Type 1 diabetes.

Provided by University at Buffalo

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