Stem Cells Show Promise as Type 2 Diabetes Treatment

Miriam E Tucker July 20, 2015

By targeting inflammation, adult allogeneic bone-marrow–derived mesenchymal precursor cells (MPCs) may represent a novel treatment for type 2 diabetes, a new pilot study suggests.

Findings from the multicenter dose-escalating randomized placebo-controlled trial in 61 adults with inadequately controlled type 2 diabetes were [published online](http://care.diabetesjournals.org/content/early/2015/07/01/dc14-2830.abstract) July 7 inDiabetes Care by Jay S Skyler, MD, deputy director for clinical research and academic programs at the Diabetes Research Institute, Miami, Florida, and colleagues.

Given as a single intravenous infusion, the cell product, called rexlemestrocel-L (Mesoblast) produced no serious adverse events over the subsequent 12 weeks, including anti-HLA antibodies or sensitization. And the agent was associated with significant reductions in HbA1c compared with placebo infusion.

"This is just a preliminary study. There was no safety issue, which is good, and there may be some beneficial effect….It wasn't powered for that but showed there might be. We're pretty excited about that," Dr Skyler told Medscape Medical News.

He noted that mesenchymal stem cells are "a hot issue at the moment," because of their anti-inflammatory effects, and that they are being studied for a variety of conditions.

"Type 2 diabetes, because there's a significant inflammatory component, is an obvious one to look at....There's evidence that if you reduce inflammation you might get beta cells to work better and you certainly lessen insulin resistance."

Asked to comment, Allison B Goldfine, MD, head of the section of clinical research at Joslin Diabetes Center, Boston, Massachusetts, said: "This is an extremely interesting proof-of-concept study....Initial human exposures did not reveal major adverse safety signals, but the number of persons exposed was small and each participant received only one dose."

She added that "mechanistically, the investigators hypothesize that the MPCs change inflammatory mediators of disease but do not show changes in the measured cytokines in these small cohorts."

Nonetheless, Dr Goldfine called the findings "overall, very preliminary but very exciting."

**No Safety Problems Seen**

The study subjects, from 18 US centers, all had type 2 diabetes and HbA1c levels of 7.0% or higher despite treatment with metformin alone or in combination with another oral glucose-lowering drug (not a thiazolidinedione).

They were randomized to receive single IV infusions of 0.3 x 106/kg of the cell product (n = 15), 1.0 x 106/kg (n = 15), 2.0 x 106/kg (n = 15) or placebo (n = 16).

No adverse events were reported during infusion or in the following 6 hours. In all, 27 (44.3%) subjects experienced adverse events over the subsequent 12 weeks, including six (40.0%) with the lowest rexlemestrocel-L dose, 10 (66.7%) with the middle dose, and five (33.3%) with the highest dose, compared with six (37.5%) in the placebo group.

One patient in the lowest-rexlemestrocel-L–dose group experienced severe abdominal pain. Other treatment-emergent adverse events, including upper-respiratory infection in two patients, were mild or moderate in severity. None discontinued the study because of an adverse event.

None of the patients developed antibodies to the cell-donor HLA, and there were no trends in changes in anti-HLA antibody responses across dose groups or over time, Dr Skyler and colleagues report.

**Exploratory Efficacy**

Numerical decreases in HbA1c levels occurred in each of the rexlemestrocel-L dose groups at all points after week 1, whereas a small increase in HbA1c occurred in the placebo group. The greatest difference between rexlemestrocel-L and placebo, 0.4 mmol/mol, occurred at week 8 (P< .05).

At week 12, the HbA1c target of less than 7% was achieved by two (13.3%) subjects in the lowest-rexlemestrocel-L–dose group, one (6.7%) in the middle-dose group, and five (33.3%) in the highest-dose group, whereas none of the placebo patients achieved that goal (P< .05 for the highest dose vs placebo).

However, there were no differences in fasting plasma glucose levels across treatment groups.

Dr Goldfine commented, "It is provocative that this limited exposure was able to detect glycemic lowering based on HbA1c. No change in fasting glucose was observed, suggesting potential postprandial effects. I am not sure what to make of the changes detected as early as 1 week. It would have been nice to have a second measure of glycemia concordant with HbA1c, such as glycated albumin."

Dr Goldfine, who [has studied](http://www.medscape.com/viewarticle/807407) another anti-inflammatory agent, salsalate, for the treatment of type 2 diabetes, noted that the current study "does add further support for the inflammatory hypothesis as an important and targetable mechanism to treat and prevent [type 2 diabetes]."

Dr Skyler told Medscape Medical News that his team is now planning a full-scale trial of rexlemestrocel-L.

And Dr Goldfine has just completed a small 30-month study of salsalate in patients with stable coronary heart disease. "I hope to be able to present these findings in the near future," she told Medscape Medical News.

Dr Skyler is a consultant to Mesoblast, which funded the study. In addition, he is supported by the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institutes of Health; he has served as a board member for Amylin Pharmaceuticals, Dexcom, Moerae Matrix, and Paean Therapeutics; he has received consulting fees from BD Technologies, Boehringer Ingelheim, Bristol-Myers Squibb, Cebix, DiaVacs, Elcelyx, Exsulin, Gilead Sciences, Halozyme Therapeutics, Ideal Life, Intarcia Therapeutics, MannKind, Mellitech, Merck, Orgenesis, Sanofi, Sekris Biomedical, Takeda, Valeritas, and ViaCyte; he has received research funding from Halozyme Therapeutics, Intuity Medical, Mesoblast, and Osiris Therapeutics; he has received speaker honoraria from Novo Nordisk and Sanofi; he has received royalties for editing a book from Springer; and he is a stockholder of Amylin Pharmaceuticals, Dexcom, Ideal Life, Moerae Matrix, OPKO Health, Patton Medical Devices, and Tandem Diabetes Care. Disclosures for the coauthors are listed in the article. Dr Goldfine is supported by the National Institutes of Health, the American Diabetes Association, and investigator-initiated multicenter work funded to Cleveland Clinic from Ethicon and Covidien. She receives supplies from Amneal Pharmaceuticals, Caraco Pharmaceuticals, Novo Nordisk, and Lifescan and assay support from Boston Health Diagnostics. She has consulted for the Colorado Prevention Center, Novo Nordisk, Boston Health Diagnostics, and institutionally with Kowa Pharmaceuticals, Novella, and Diasome.