placebo responders (69.2% vs 44.4%, respectively) than in liraglutide and placebo nonresponders (67.2% vs 39.6%, respectively). Responders had lower rates of AEs leading to withdrawal (liraglutide, 4.5%; placebo, 0.9%). In nonresponders, the figures were 17% for liraglutide vs 4.8% for placebo.

Liraglutide responders had greater improvements than nonresponders across a range of efficacy outcomes. Overall, weight loss ≥ 5% was achieved in a higher proportion of patients on liraglutide, 3 mg, with a stronger effect among responders. The rates of AEs were largely equivalent in responders and nonresponders.

A mean weight loss of 11.7% was achieved by patients who were overweight or obese without diabetes and responded to liraglutide. The weight loss responders in both treatment groups also had improved glycemic, cardiometabolic, and health-related quality-of-life outcomes. The SCALE–Obesity and Prediabetes trial showed that liraglutide is a safe and effective weight loss option in the study population.

Significant HbA_{1c} Reduction With Empagliflozin/ Linagliptin Combination

Written by Rita Buckley

One tablet of empagliflozin and linagliptin significantly reduced HbA_{1c} in patients with type 2 diabetes. Andrew J. Lewin, MD, National Research Institute, Los Angeles, California, USA, and colleagues conducted a randomized, double-blind, parallel-group, phase 3 study, the Safety and Efficacy of the Combination of Empagliflozin and Linagliptin Compared to Linagliptin Alone Over 24 Weeks in Patients With Type 2 Diabetes study [Lewin A et al. *Diabetes Care*. 2015].

Empagliflozin reduces renal glucose reabsorption, thereby increasing urinary glucose excretion. This leads to a decline in plasma glucose levels in an insulin-independent manner [Heise T et al. *Diabetes Obes Metab*. 2013]. Linagliptin prevents the inactivation of incretin peptides, such as glucagon-like peptide-1 (GLP-1), stimulates insulin release, and inhibits glucagon secretion [Gallwitz B. *Diabetes Metab Syndr Obes*. 2013]. Each drug is an FDA-approved treatment for patients with type 2 diabetes. As compared with the single agent treatment groups, those treated with the dual combination achieved lower A_{1c} levels.

Efficacy was evaluated in 667 patients who had not received antihyperglycemic therapy for ≥ 12 weeks. Their mean (standard deviation) age was 54.6 (10.2) years; mean weight was 87.9 (20.1) kg; average body mass index was 31.6 (5.6) kg/m^2; and mean HbA_{1c} level was 8.02% (0.96). Baseline characteristics were balanced between treatment groups.

Patients were randomized (1:1:1:1:1) to receive empagliflozin 25 mg/linagliptin 5 mg as a fixed-dose combination (FDC) tablet; empagliflozin 10 mg/linagliptin 5 mg as an FDC tablet; empagliflozin 25 mg; empagliflozin 10 mg; or linagliptin 5 mg for 52 weeks. The primary end point was the change from baseline in HbA_{1c} at week 24.

At week 24, reductions from baseline in HbA_{1c} were significantly greater for empagliflozin 25 mg/linagliptin 5 mg compared with linagliptin 5 mg ($P<.001$), but not compared with empagliflozin 25 mg ($P<.179$), and were significantly greater for empagliflozin 10 mg/linagliptin 5 mg compared with individual doses ($P<.001$ for both). At week 24, 55.4% of patients with baseline $HbA_{1c} \geq 7\%$ reached $HbA_{1c} < 7\%$ with empagliflozin 25 mg/linagliptin 5 mg; 62.3% did so with empagliflozin 10 mg/linagliptin 5 mg; 41.5% with empagliflozin 25 mg; 38.8% with empagliflozin 10 mg; and 32.3% with linagliptin 5 mg. Efficacy was maintained at week 52.

The proportion of patients with adverse events over this time was similar across groups (68.9% to 81.5%), with no confirmed hypoglycemic adverse events in either combination group. Empagliflozin/linagliptin was well-tolerated, with an overall safety profile similar to those of the individual drugs.

This was the first randomized controlled trial to evaluate the efficacy and safety of the initial combination of a sodium-glucose cotransporter 2 (SGLT2) inhibitor (empagliflozin) and a DPP-4 inhibitor (linagliptin) in patients with type 2 diabetes.

ATL1103 Effective in Reducing IGF-1 Levels in Patients With Acromegaly

Written by Jill Shuman

Acromegaly is a chronic disorder resulting from excessive secretion of growth hormone, with a resulting increase in the production of the hormone known as insulinlike growth factor 1 (IGF-1). ATL1103 is a second-generation antisense drug designed to silence growth hormone receptor expression, thereby reducing levels of IGF-1 in the blood. It is currently under investigation as a potential treatment for diseases associated with excessive growth hormone action, such as acromegaly [Störmann S, Schopohl J. *Expert Opin Emerg Drugs*. 2014].

Peter J. Trainer, MD, The Christie National Health Service Foundation Trust, Manchester, United Kingdom, reported primary efficacy results from the phase 2 clinical trial of ATL1103 in patients with acromegaly [2012-003147-30]. The ATL1103 phase 2 trial was a randomized, open-label, multicenter, parallel group study