## Albiglutide Superior to Sitagliptin and Glimepiride in T2DM

Written by Emma Hitt, PhD

Treatment with albiglutide in combination with metformin was superior to sitagliptin and glimepiride for reduction of HbA1C and fasting plasma glucose (FPG) levels in patients with type 2 diabetes mellitus (T2DM). Murray Stewart, MD, GlaxoSmithKline, Upper Merion, Pennsylvania, USA, presented data from the Efficacy and Safety of Albiglutide in Treatment of Type 2 Diabetes trial [HARMONY 3; NCT00838903].

A long-acting glucagon-like peptide 1 receptor agonist, albiglutide is being evaluated in patients with T2DM in a series of 8 trials. The purpose of the HARMONY 3 trial was to determine the efficacy and safety of albiglutide compared with placebo, sitagliptin, or glimepiride in patients with T2DM currently taking metformin.

In the double-blind Phase 3 HARMONY 3 trial, 1012 patients were randomized to receive 30 mg of once-weekly albiglutide, 100 mg of once-daily sitagliptin, 2 to 4 mg of once-daily glimepiride, or placebo once weekly for 104 weeks. All patients received up to 1 g of metformin. The mean age at study initiation was 54.5 years and at baseline patients had a mean body mass index (BMI) of 32.6 kg/m$^2$, mean weight of 90.7 kg, and a mean 6 years of diabetes duration [Johnson S et al. EASD 2013 (abstr 5)].

The primary endpoint of the HARMONY 3 study was HbA1C change from baseline at 104 weeks. The secondary endpoints included change in HbA1C from baseline over time, change in FPG over time, change in body weight from baseline over time, proportion of patients that reached the HbA1C goal, and time to hypoglycemia rescue.

Patients treated with albiglutide demonstrated a mean –6.89 change in HbA1C from baseline (95% CI, –8.31 to –5.57), treatment with sitagliptin resulted in a –3.06 change (95% CI, –4.48 to –1.64), and treatment with glimepiride resulted in a –3.94% change (95% CI, –5.36 to –2.62), compared with a 2.95% change from baseline in patients treated with placebo (95% CI, 0.55 to 5.47). Albiglutide treatment resulted in a significant decrease in FPG compared with sitagliptin (–0.86; 95% CI, –1.30 to –0.41; p=0.0002), glimepiride (–0.56; 95% CI, –1.01 to –0.12; p=0.0133), and placebo (–1.53; 95% CI, –2.16 to –0.90; p<0.0001).

Adverse events were similar among treatment groups and included nausea, diarrhea, and vomiting. Injection-site reactions occurred in 17.2% of patients in the albiglutide arm, 6% in the sitagliptin arm, 8% in the glimepiride arm, and 5% in the placebo arm. There were no severe hypoglycemic events; however, prerescue documented symptomatic hypoglycemia was reported in 3%, 2%, and 18% of patients treated with albiglutide, sitagliptin, and glimepiride, respectively, compared with 4% of patients who received placebo.

Pancreatitis occurred in four patients who received albiglutide and two patients who received glimepiride; pancreatitis was determined to be possibly associated to the study drug in two patients who received albiglutide. In addition, one patient treated with albiglutide and two patients treated with sitagliptin developed thyroid cancer during the study.

Dr. Stewart indicated that, in his opinion, the data from the HARMONY 3 trial suggest that albiglutide in combination with metformin was superior to add-on therapy with sitagliptin or glimepiride for a decrease in HbA1C and FPG.

## Once-Weekly Dulaglutide Produces Superior Glycemic Control Compared With Metformin

Written by Brian Hoyle

Efficacy and safety data from the Impact of LY2189265 Versus Metformin on Glycemic Control in Early Type 2 Diabetes Mellitus: Assessment of Weekly Administration of LY2189265 in Diabetes-3 study [AWARD-3; NCT01126580] Phase 3, randomized, double-blind, parallel-arm, monotherapy study have revealed the superiority of once-weekly dulaglutide 0.75 or 1.5 mg compared with twice-daily metformin 1000 mg in controlling glycemia in type 2 diabetes. The AWARD-3 results were presented by Santiago Tofé Povedano, MD, Clinica Juaneda, Palma de Mallorca, Spain.

Dulaglutide is a long-acting glucagon-like peptide-1 receptor agonist. The study compared two doses of dulaglutide administered once weekly to metformin administered twice daily in 807 patients with early type 2 diabetes (mean duration 2.6 years). Prior to inclusion in this study, the patients had been treated by diet and exercise alone or along with a low dose of an oral antidiabetic drug taken for ≥3 months.

The primary hypothesis was that dulaglutide 1.5 mg is noninferior to metformin with respect to the change in HbA1C from baseline to 26 weeks. Secondary hypotheses of note were that the higher dose of dulaglutide (1.5 mg) is superior to metformin and that the lower dulaglutide dose (0.75 mg) is noninferior and/or superior to metformin.

The results at 26 and 52 weeks in the intention-to-treat population are summarized in Table 1. In terms of the change in HbA1C from baseline, both dulaglutide doses and the higher dose were superior to metformin at 26 weeks and 52 weeks, respectively.