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.

Table 1. Summary of Efficacy Results at Primary and Final Time Points

Primary Time Point (26 Weeks, ITT, LOCF)	DU 1.5 mg (n=269)	DU 0.75 mg (n=270)	MET 2000 mg (n=268)
HbA1C change (%), LS mean (SE)	–0.78 (0.06)††	–0.71 (0.06)††	–0.56 (0.06)
Patients with HbA1C <7% (%)	61.5*	62.6*	53.6
Weight change (kg), LS mean (SE)	–2.29 (0.24)*	–1.36 (0.24)*	–2.22 (0.24)
Final Time Point (52 Weeks, ITT, LOCF)			
HbA1C change (%), LS mean (SE)	–0.70 (0.07)††	–0.55 (0.07)†	–0.51 (0.07)
Patients with HbA1C <7% (%)	60.0*	53.2	48.3
Weight change (kg), LS mean (SE)	–1.93 (0.29)	–1.09 (0.29)*	–2.20 (0.29)

DU=dulaglutide; ITT=intention-to-treat; LOCF=last observation carried forward; LS=least squares; MET=metformin; SE=standard error. *2-sided p<0.05 vs MET. † and †† multiplicity adjusted 1-sided p<0.025 for noninferiority or superiority, respectively, vs MET, for HbA1C change only.

Tofé Povedano S et al. EASD 2013 (abstr 4).

The incidence of adverse events was 6.0% for metformin, which was less than the rate (7.4%) of the dulaglutide 0.75 mg, but greater than the rate (5.2%) of the dulaglutide 1.5 mg. Gastrointestinal-related adverse events occurred frequently for patients treated with dulaglutide 1.5 mg, followed by metformin, followed by dulaglutide 0.75 mg. At 52 weeks, the percentage of patients with systematic hypoglycemia (defined as <3.9 mmol/L) was 6.3% for those receiving the higher dose of dulaglutide, 5.9% for those receiving the lower dose of dulaglutide, and 4.9% for those receiving metformin (overall p=0.756) [Tofé Povedano S et al. EASD 2013 (abstr 4)].

The findings demonstrated the superior glycemic control of both doses of dulaglutide given once-a-week compared with metformin administered twice each day. In addition, dulaglutide was well tolerated.

Type 1 Diabetes Impairs Education and Employment

Written by **Emma Hitt, PhD**

Childhood onset type 1 diabetes mellitus (T1DM) is associated with lower education, lower rates of employment, and lower employment earnings in both men and women in Sweden. Sofie Persson, MD, Lund University, Malmö, Sweden, presented data from a registry study of young adults with childhood onset T1DM.

Although the effect of T1DM on socioeconomic status is not well understood, lifestyle changes and complications related to childhood onset T1DM may result in greater rates of absenteeism and can decrease work capacity [Persson S et al. EASD 2013 (abstr 39)]. A previous study suggested that childhood onset T1DM had a negative impact on compulsory and secondary education [Persson S et al. *Diabetologia* 2013]. The purpose of this registry study was to examine the effect of childhood onset T1DM on rates of university-level education and labor market outcomes in early adulthood.

The study included 2485 patients in the Swedish Childhood Diabetes Register that were born between 1972 and 1978 and were diagnosed with T1DM at <15 years. The Swedish Childhood Diabetes Register is linked to other national registers, including the longitudinal integration database for health insurance and labor market studies (LISA). In addition, 9940 controls matched for birth year and residency at diagnosis were selected by Statistics Sweden. Annual earnings data were collected between 1990 and 2010, corresponding to ages 19 to 32 years. Statistics used in this study included linear, logistic, and panel data regression, and socioeconomic status and demographics were controlled.

Fewer women and men with childhood onset T1DM had a university-level degree at age 32 years compared with individuals from the general population (women: OR, 0.79; 95% CI, 0.69 to 0.92; men: OR, 0.81; 95% CI, 0.70 to 0.94). In addition, individuals with childhood onset T1DM were less likely to have continued their higher education for 3 or more years (women: OR, 0.79; 95% CI, 0.68 to 0.91; men: OR, 0.80; 95% CI, 0.68 to 0.94).

Rates of employment at age 32 years were lower in individuals with childhood onset T1DM compared with the general population (women: OR, 0.66; 95% CI, 0.53 to 0.81; men: OR, 0.63; 95% CI, 0.50 to 0.80). Individuals with childhood onset T1DM that were employed were likely to have lower earnings than the general population, at –13% lower for women (p=0.003) and –8% for men (p<0.002), a trend that appeared to begin in the early 20s (Figure 1). Persson pointed out that the impact of childhood onset T1DM on earnings appeared to rise with increasing duration of the disease. The negative impact was not observed until after a 16-year duration of T1DM.

Prof. Persson indicated that, in her opinion, the data from the present study suggest that childhood onset T1DM has a negative impact on earning a higher education degree, gaining employment, and earnings among young adults. In general, women with T1DM experienced the greatest negative impact. She concluded that additional research is needed to determine the impact of T1DM on the labor market over a longer time period.