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.

Figure 1. Earnings Through Early Adulthood in Patients With T1DM in Sweden

Annual earnings of women and men between 19 and 32 years of age
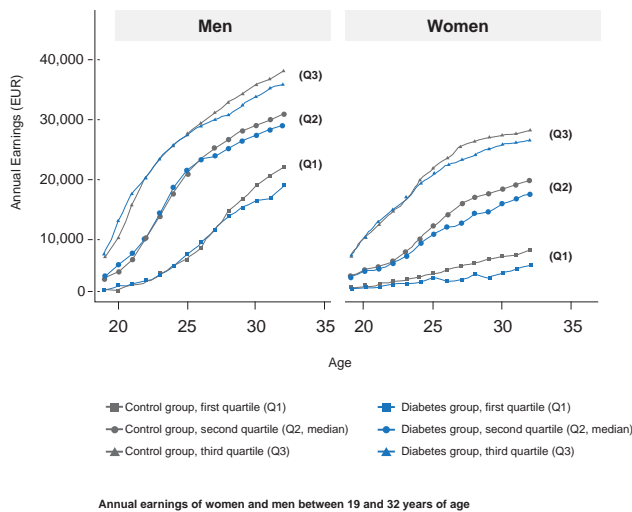
Reproduced with permission from S Persson, MD.

Long-Term Ranibizumab Effective in Diabetic Macular Edema

Written by Emma Hitt, PhD

In patients with diabetic macular edema (DME), long-term intravitreal injections of ranibizumab maintains best-corrected visual acuity (BCVA) and central retinal subfield thickness (CRT) improvements over 36 months, with no new or increased safety concerns. Anna Boixadera, MD, Hospital Vall D'Hebron, Barcelona, Spain, presented the final analysis of the 36-month study comprising: A 12 Month Core Study to Assess the Efficacy and Safety of Ranibizumab (Intravitreal Injections) in Patients With Visual Impairment Due to Diabetic Macular Edema and a 24 Month Open-Label Extension Study [RESTORE; NCT00687804].

In patients with diabetes, the most common cause of vision loss is macular edema, which is a leading cause of visual impairment in the working-age population [Ciulla TA et al. *Diabetes Care* 2003]. The RESTORE core trial demonstrated that ranibizumab treatment as monotherapy or in combination with laser therapy was superior to laser therapy alone in patients with visual impairment due to DME over 12 months [Mitchell P et al. *Ophthalmology* 2011]. The purpose of the extension study was to evaluate the long-term efficacy and safety of ranibizumab 0.5 mg intravitreal injections [Boixadera A, Garcia-Arumi J. EASD 2013 (abstr 54)].

In the open-label, multicenter RESTORE extension study, 240 patients were eligible to receive ranibizumab as

needed according to prespecified BCVA stability and DME progression-based retreatment criteria for 24 months. Laser therapy was allowed. The extension study was completed by 208 patients, and 19% and 25% of patients did not require ranibizumab injections during the extension study. The mean age of participants ranged from 61.7 to 63.8 years and the mean duration of DME ranged from 1.5 to 1.7 years.

The most common ocular adverse events (AEs) during the 36-month RESTORE core and extension studies were cataracts (16.3%) and eye pain (15.4%). Serious ocular AEs were reported in 2.4% to 4.1% of patients; there were no incidents of retinal tear or detachment, and no reports of endophthalmitis during the 36 months. The most frequent nonocular AEs included nasopharyngitis (23.3%) and hypertension (13.3%). The most frequent nonocular serious AEs included coronary artery disease and cerebrovascular accident (1.7% each).

The mean BCVA gain and CRT reductions observed from baseline to Month 12 were maintained through Month 36 in patients treated with prior ranibizumab in both the core and extension phase (+8.0 letters, –145.9 µm [prior ranibizumab], +6.7 letters, –142.1 µm [prior ranibizumab plus laser]). In addition, patients who had received laser monotherapy in the core study experienced progressive BCVA improvement (+6.0 letters) and CRT reduction (–142.7 µm) during the extension trial (Months 12 to 36) with ranibizumab treatment. The mean change in the Visual Functioning Questionnaire scores over the 36 months for the ranibizumab monotherapy, ranibizumab plus laser therapy, and laser monotherapy arms were +12.2, +7.8, and +8.4, respectively, for near activities and +2.6, +4.1, and +3.5, respectively, for distance activities, and the mean change in the composite score was +5.0, +4.3, and +3.9, respectively.

Prof. Boixadera stated that, in her opinion, the data from the RESTORE core and extension studies indicate that there are no new or increased safety issues with long-term intravitreal ranibizumab injections. In addition, patients could maintain their BCVA and CRT improvements gained in the first year of ranibizumab treatment with decreasing frequency of ranibizumab injections in subsequent years.

Left Ventricular Remodeling Reduced With Olmesartan in ROADMAP

Written by Mary Mosley

A prespecified analysis of left ventricular hypertrophy (LVH) as evaluated by electrocardiography (ECG) from the Olmesartan Medoxomil in Diabetes Mellitus study [ROADMAP] showed that olmesartan significantly