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P009

IDegLira Improves Glycemic Control in People with Type 2 Diabetes Uncontrolled on Basal Insulin Without Deterioration Despite Discontinuing Pre-trial Sulfonylurea

Friday, October 11, 2019, 10:15 – 11:15 AM, 2:25 - 3:25 PM
Saturday, October 12, 2019, 10:00 – 11:00 AM, 2:15 - 3:15 PM

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Purpose
As combining a sulfonylurea (SU) and insulin can elevate the risk of hypoglycemia, prescribers often reduce the dose of SU or discontinue SUs when initiating insulin. This can lead to a deterioration in glycemic control. The DUAL II trial compared the efficacy and safety of insulin degludec/liraglutide fixed-ratio combination (IDegLira) versus insulin degludec (degludec) (starting doses 16 units [U], maximum doses 50 U), both plus metformin, in people with type 2 diabetes (T2D) with poor glycemic control previously treated with metformin +/- SU/glinides and basal insulin (20–40 U). This subgroup analysis compared clinical findings in people discontinuing SU (pre-trial SU users) with those in people not taking SU pre-trial (non-SU users).

Methods
Change from baseline in HbA1c, fasting plasma glucose (FPG) and body weight, and end of trial (EOT) insulin dose after 26 weeks of treatment were analyzed with an analysis of covariance (ANCOVA) model. Region, pre-trial use of SU at screening, randomized treatment, and interaction between pre-trial use of SU and randomized treatment, were fixed factors and baseline value was covariate (and baseline HbA1c for insulin dose). Treatment-emergent confirmed hypoglycemia was analyzed using a negative binomial regression model with a log link and the logarithm of the time period in which a hypoglycemic episode was considered treatment-emergent as offset, and the same fixed effects as the ANCOVA model. Missing data were imputed using last observation carried forward.

Results
Mean (standard deviation; SD) change from baseline to Week 26 in HbA1c with IDegLira vs degludec was -1.7 (1.2) vs -0.6 (1.1)% (estimated treatment difference; ETD [95% CI] -1.13 [-1.41;-0.84]) in pre-trial SU users (n=198) and -2.1 (1.0) vs -1.2 (1.2)% (-0.94 [-1.23;-0.66]) in non-SU users (n=200). Mean (SD) change from baseline to Week 26 in FPG with IDegLira vs degludec was -58.8 (56.8) vs -43.3 (59.6) mg/dL (ETD [95% CI] -17.03 [-28.66;-5.39]) in pre-trial SU users and -66.1 (48.2) vs -49.5 (60.0) mg/dL (-9.36 [-21.05;2.32]) in non-SU users. Mean (SD) change from baseline to Week 26 in body weight with IDegLira vs degludec was -3.1 (3.6) vs -0.3 (2.6) kg (ETD [95% CI] -2.77 [-3.75;-1.79]) in pre-trial SU users and -2.3

(3.8) vs 0.3 (4.0) kg (-2.41 [-3.39;-1.43]) in non-SU users. Baseline daily insulin dose was 26.8–27.5 U in pre-trial SU users and 30.6–31.5 U in non-SU users, and mean (SD) EOT dose with IDegLira vs degludec was 43.9 (10.2) vs 44.9 (9.3) U (ETD [95% CI] -0.80 [-3.39;1.79]) in pre-trial SU users and 45.8 (8.5) vs 44.9 (9.7) U (ETD 1.09 [-1.52;3.69]) in non-SU users. Treatment effect was consistent across groups, with no statistically significant subgroup interactions (HbA1c, p=0.3828; FPG, p=0.3618; body weight, p=0.6137; EOT daily insulin dose, p=0.3132). A non-clinically relevant increase in mean self-measured fasting plasma glucose (SMPG) occurred in Weeks 0–3 in pre-trial SU users, returning to baseline by Week 4. Mean SMPG decreased from baseline to EOT with IDegLira in non-SU users. Number of hypoglycemic events per patient-year of exposure with IDegLira vs degludec was 1.7 vs 3.0 (estimated rate ratio; ERR [95% CI] 0.56 [0.26;1.22]) in pre-trial SU users and 1.4 vs 2.3 (ERR 0.88 [0.41;1.92]) in non-SU users (subgroup interaction p=0.4221).

Conclusions

In people who reduced their insulin dose and discontinued SU at IDegLira initiation, no clinically relevant deterioration in glycemic control was seen. For all endpoints analyzed, regardless of SU use pre-trial, IDegLira showed better results in all metabolic parameters versus degludec (both with a maximum dose of 50 U). The clinical findings were consistent between pre-trial SU users and non-SU users.