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Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients With Type 2 Diabetes
The SWITCH 2 Randomized Clinical Trial

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IMPORTANCE Hypoglycemia, a serious risk for insulin-treated patients with type 2 diabetes, negatively affects glycemic control.

OBJECTIVE To test whether treatment with basal insulin degludec is associated with a lower rate of hypoglycemia compared with insulin glargine U100 in patients with type 2 diabetes.

DESIGN, SETTING, AND PARTICIPANTS Randomized, double-blind, treat-to-target crossover trial including two 32-week treatment periods, each with a 16-week titration period and a 16-week maintenance period. The trial was conducted at 152 US centers between January 2014 and December 2015 in 721 adults with type 2 diabetes and at least 1 hypoglycemia risk factor who were previously treated with basal insulin with or without oral antidiabetic drugs.

INTERVENTIONS Patients were randomized 1:1 to receive once-daily insulin degludec followed by insulin glargine U100 (n = 361) or to receive insulin glargine U100 followed by insulin degludec (n = 360) and randomized 1:1 to morning or evening dosing within each treatment sequence.

MAIN OUTCOMES AND MEASURES The primary end point was the rate of overall symptomatic hypoglycemic episodes (severe or blood glucose confirmed [<56 mg/dL]) during the maintenance period. Secondary end points were the rate of nocturnal symptomatic hypoglycemic episodes (severe or blood glucose confirmed, occurring between 12:01 AM and 5:59 AM) and the proportion of patients with severe hypoglycemia during the maintenance period.

RESULTS Of the 721 patients randomized (mean [SD] age, 61.4 [10.5] years; 53.1% male), 580 (80.4%) completed the trial. During the maintenance period, the rates of overall symptomatic hypoglycemia for insulin degludec vs insulin glargine U100 were 185.6 vs 265.4 episodes per 100 patient-years of exposure (PYE) (rate ratio = 0.70 [95% CI, 0.61-0.80]; $P < .001$; difference, −23.66 episodes/100 PYE [95% CI, −33.98 to −13.33]), and the proportions of patients with hypoglycemic episodes were 22.5% vs 31.6% (difference, −9.1% [95% CI, −13.1% to −5.0%]). The rates of nocturnal symptomatic hypoglycemia with insulin degludec vs insulin glargine U100 were 55.2 vs 93.6 episodes/100 PYE (rate ratio = 0.58 [95% CI, 0.46-0.74]; $P < .001$; difference, −7.41 episodes/100 PYE [95% CI, −11.98 to −2.85]), and the proportions of patients with hypoglycemic episodes were 9.7% vs 14.7% (difference, −5.1% [95% CI, −8.1% to −2.0%]). The proportions of patients experiencing severe hypoglycemia during the maintenance period were 1.6% (95% CI, 0.6%-2.7%) for insulin degludec vs 2.4% (95% CI, 1.1%-3.7%) for insulin glargine U100 (McNemar $P = .35$; risk difference, −0.8% [95% CI, −2.2% to 0.5%]). Statistically significant reductions in overall and nocturnal symptomatic hypoglycemia for insulin degludec vs insulin glargine U100 were also seen for the full treatment period.

CONCLUSIONS AND RELEVANCE Among patients with type 2 diabetes treated with insulin and with at least 1 hypoglycemia risk factor, 32 weeks' treatment with insulin degludec vs insulin glargine U100 resulted in a reduced rate of overall symptomatic hypoglycemia.

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