Once Weekly Basal Insulin Fc (BIF) is Safe and Efficacious in Patients with Type 2 Diabetes Mellitus (T2DM) Previously Treated With Basal Insulin

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Abstract: Basal insulin Fc (BIF; LY3209590) is a novel, once-weekly, long-acting IgG Fc-fusion protein that is being assessed for the treatment of diabetes mellitus. The presented study evaluated the safety and efficacy of BIF compared to insulin degludec over 32 weeks in patients with T2DM previously treated with oral antidiabetic drugs and a basal insulin. The study design included 2 different dosing algorithms for BIF (BIF-A1 and BIF-A2) with two different fasting glucose (FG) targets of ≤140 mg/dL (BIF-A1) and ≤120 mg/dL (BIF-A2). Insulin degludec was titrated to a FG target of ≤100mg/dL using a modified Riddle treat-to-target algorithm. Study participants (N=399) were randomized in a 1:1:1 ratio to 1 of 3 parallel treatment groups. The average age of participants was 60.2 years, baseline HbA1c was 8.1% and duration of diabetes 14.7 years. There were no statistically significant differences in demographics or baseline characteristics across the 3 treatment groups. Both BIF groups achieved non-inferiority (non-inferiority margin = 0.4%) for the primary endpoint of HbA1c change from baseline to Week 32 with a mean±SE reduction for BIF-A1, BIF-A2 and insulin degludec of 0.6±0.1%, 0.6±0.1% and 0.7±0.1%, respectively. In line with the different fasting serum glucose (FSG) targets, insulin degludec achieved greater FSG lowering from baseline as compared to the BIF arms. Similarly, both BIF dosing groups showed significantly fewer hypoglycemic events compared to insulin degludec (all documented events as well as nocturnal events) when assessing events ≤70 mg/dL (3.9 mmol/L). Hypoglycemic events <54 mg/dL (3.0 mmol/L - all documented events as well as nocturnal events) were not significantly different between the three dosing groups. Two severe hypoglycemic events were reported in BIF-A2. The reported treatment-emergent adverse events and serious adverse events were balanced across the 3 treatment groups. Both BIF groups had a statistically significantly smaller increase in body weight compared to insulin degludec from baseline to Week 32. In summary, BIF, when administered weekly according to either dosing algorithm, was noninferior to insulin degludec for glycemic control as measured by change in HbA1c after 32 weeks with a lower rate of documented and nocturnal hypoglycemia ≤70 mg/dL and less weight gain. Additionally, no safety signals were detected. While higher FG targets were chosen in this first Phase 2 study with BIF, the safety and tolerability results allow assessment of lower target glucose ranges in future trials. The results from this study support continued development of BIF as a once-weekly insulin treatment of diabetes mellitus.

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