Efficacy of iGlarLixi in patients with type 2 diabetes and high HbA1c or who have failed to reach HbA1c targets on two oral antihyperglycemic drugs

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Video Abstract

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Abstract

Worldwide, many patients treated for type 2 diabetes are not achieving their recommended glycemic targets. For patients with very poorly controlled diabetes, such as those with an HBA1C more than 2% above their target or with HbA1c over 10%, the ADA and EASD consensus recommendations include combination therapy with both basal insulin and a glucagon-like peptide-1 receptor agonist (or GLP-1 RA). iGlarLixi is a once-daily, titratable, fixed-ratio combination of basal insulin glargine 100 units (or glargine) and lixisenatide, a GLP-1 RA. The complementary mechanisms of action of lixisenatide and glargine means that this combination targets both fasting and post-prandial hyperglycemia with a single injection. To examine whether iGlarLixi is a therapeutic option for patients with very poorly controlled type 2 diabetes, the authors of the current study analyzed two sub-groups of the LixiLan-O clinical trial. Their findings are published in Diabetes, Obesity and Metabolism. In LixiLan-O, patients with type 2 diabetes uncontrolled on metformin with or without a second oral antihyperglycemic drug, achieved greater reductions in H-b-A-1-c with iGlarLixi treatment versus either glargine or lixisenatide alone. This benefit was seen without increases in either hypoglycemia or weight versus glargine, and with low gastrointestinal side effects compared with lixisenatide. In this exploratory analysis, the effects of iGlarLixi, compared with either glargine or lixisenatide alone, was analyzed in LixiLan-O patients with HbA1c levels of at least 9% at baseline and those with inadequate glycemic control, defined as HbA1c levels of 7% to 9%, who were on metformin and a second antihyperglycemic drug at screening. In both patient subgroups, iGlarLixi yielded significantly greater HbA1c reductions than did either glargine or lixisenatide alone: 2.9%, 2.5% and 1.7%, respectively, in the high-H-b-A-1-c subgroup; and 1.5%, 1.2%, and 0.7%, respectively, in the subgroup on two oral antihyperglycemic drugs. In both subgroups over 70% of patients treated with iGlarLixi reached HbA1c levels below 7%. iGlarLixi also mitigated the weight gain observed with glargine alone, and the overall rates of clinically important hypoglycemia were low. Rates of gastrointestinal treatment-emergent adverse events were lower with iGlarLixi versus lixisenatide, although they were higher versus glargine in both subgroups. One limitation of this post hoc subgroup analysis was that the original trial was not designed to detect differences between treatments in the two subgroups examined. In addition, the high-HbA1c subgroup was rather small. Patients with HbA1c over 9% are often under-represented in clinical trials and need further study in a larger trial population. The achievement of HbA1c less than 7% in over 70% of patients, low rates of hypoglycemia and avoidance of weight gain with a single injection suggest that iGlarLixi could serve as an effective option for treatment intensification in these difficult-to-treat patient groups.