Brief Communication

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Insulin/GLP-1 Treatment for Patients with DM

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Combining basal insulin therapy with a glucagon-like peptide-1 receptor agonist (GLP-1 RA) has clear clinical advantages, and is supported by the latest EASD/ADA position statement (1). IDegLira is a once-daily combination of the basal insulin, degludec, and the GLP-1RA, liraglutide, in one pen. The DUAL phase 3 clinical trial program provides important evidence about the efficacy and safety of IDegLira in three different populations of patients with type 2 diabetes (T2D): insulin naïve subjects uncontrolled on oral antidiabetic drugs (OADs), subjects uncontrolled on OAD(s) and a GLP-1 RA, and subjects uncontrolled on OAD(s) and basal insulin. Treatment with IDegLira reduced mean HbA1c to below the EASD/ADA treatment target of 7.0% in all five trials. The mean reduction of HbA1c from baseline ranged from 1.3% and 1.9%. IDegLira resulted in weight loss for subjects uncontrolled on basal insulin, was weight neutral for subjects on OADs and weight gain was minimal (2 kg) for subjects previously treated with a GLP-1 RA. Rates of hypoglycaemia were low across all the trials, particularly considering the level of glycaemic control achieved.

Keywords: Insulin, GLP-1 receptor agonist, Prader-Willi syndrome, Diabetes mellitus

The prevalence of type 2 diabetes mellitus (DM2) is rising. Hence, there is a growing need for a patient-tailored therapy. It is important to adjust therapy throughout the disease spectrum in order to achieve adequate glycemic control as defined by the EASD/ADA position statement[1].

Liraglutide is an once-daily GLP-1-RA that has a 97% structural homology to human GLP1[2]. Liraglutide efficacy and safety have been investigated in the 'Liraglutide Effect and Action in Diabetes' (LEAD) trials, where it was demonstrate that Liraglutide improves glycemic control, and also has a beneficial effects on body weight and blood pressure[2]. In the recently published LEADER trial cardiovascular safety was confirmed and in addition cardio protection was also confirmed[3].

Insulin degludec (IDeg) is a new basal insulin, which is formulated as di-hexamers with phenol and zinc. The di-hexamers will self-associate after subcutaneous injection to form a depot of soluble multihexamers. From this depot, monomers will gradually dissociate and be absorbed in the circulation, where they bind reversibly to albumin, giving it a stable concentration and duration of action for >42 h, with a half-life of 25 h[4]. Insulin Degludec was investigated in the Begin program.

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The DUAL clinical development program consists of 6 reported trials and 3 trials ongoing.

The data from the DUAL program demonstrates that IDegLira effectively improves glycemic control with a low rate of hypoglycemia and with weight neutrality or even weight loss and there by mitigates the potential side effects of its monocomponents.

In terms of safety no new safety signals were identified and specifically in terms of nausea, only very low rates were observed[5].

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