

## EFFECTS OF EXENATIDE COMPARED WITH TWICE-DAILY BIPHASIC INSULIN ASPART IN PATIENTS WITH TYPE 2 DIABETES USING METFORMIN AND A SULPHONYLUREA

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In patients with type-2 diabetes (T2D) inadequately treated with oral antidiabetic agents (OADs), studies have shown that exenatide treatment significantly improves glycaemic control with the added benefit of weight reduction. Alternative treatment options include insulin with a formulation containing both intermediate and rapid-acting components. We conducted a 1-y trial to compare the safety and efficacy of exenatide and biphasic insulin aspart (BIA) 30/70 in patients inadequately treated with metformin (MET) and a sulphonylurea (SU). 66 sites in 13 countries participated in this open-label trial. Intention-to-treat patients with T2D (mean $\pm$ SD: age 58.7 $\pm$ 9.0y, HbA<sub>1c</sub> 8.6 $\pm$ 1.0%, BMI 30.4 $\pm$ 4.1kg/m<sup>2</sup>, body weight 84.4 $\pm$ 15.7kg) were randomised to exenatide (n=253; 5 $\mu$ g BID for 4wks, 10 $\mu$ g BID thereafter) or BIA (n=248; BID doses individually titrated), adjunctive to pre-existing SU/MET treatment. The primary endpoint in this noninferiority trial was change in HbA<sub>1c</sub> at Wk 52. The noninferiority margin for the difference between treatments was 0.4%. The mean dose of BIA increased from 15.7U/d (Wk 2) to 24.4U/d (Wk 52). Both treatments resulted in reductions in HbA<sub>1c</sub> at endpoint (mean $\pm$ SEM: exenatide -1.04 $\pm$ 0.07%, BIA -0.89 $\pm$ 0.06%; difference -0.15% [95% CI -0.32 to +0.01%]). A greater proportion of E-treated patients achieved target HbA<sub>1c</sub>  $\leq$ 6.5% (E 18%, BIA 9%; between-group p=.002) and target HbA<sub>1c</sub>  $\leq$ 7% (E 32%, BIA 24%; between-group p=.078). E-treated patients experienced a steady decline in body weight (-2.5 $\pm$ 0.2Kg, p<.001), while those receiving BIA gained weight (+2.9 $\pm$ 0.2Kg, p<.001), for a difference between treatments of -5.4Kg (95% CI -5.9 to -5.0Kg, p<.001). Both treatments reduced fasting serum glucose (E -1.8 $\pm$ 0.2 mM, p<.001; BIA -1.6 $\pm$ 0.2 mM, p<.001). Between-group analyses revealed greater reductions in 2-h postbreakfast and 2-h postdinner glucose concentrations in the exenatide group, while BIA predominantly reduced premeal glucose. Nausea (33% incidence, 3.5% withdrawal rate) and vomiting (15% incidence, 1.6% withdrawal rate), mostly mild/moderate intensity, were the most common adverse events reported by E-treated patients. Hypoglycaemia rates were not significantly different between treatment groups (E 4.7 $\pm$ 0.7 events/patient-y, BIA 5.6 $\pm$ 0.7 events/patient-y). No severe hypoglycaemia was reported. E-treatment resulted in overall glycaemic control similar to conventional insulin treatment with BIA, but without the inconvenience of ongoing titration. Nausea and vomiting were not a significant cause of patient discontinuation from the study. Exenatide reduced fasting glucose, provided better postprandial glucose control, and was associated with weight reduction, making it a potential alternative to BIA for the treatment of T2D not adequately treated with OADs.