Oral presentation 17

Efficacy and safety of fast-acting insulin aspart compared with insulin aspart, both with insulin degludec with or without metformin, in adults with type 2 diabetes

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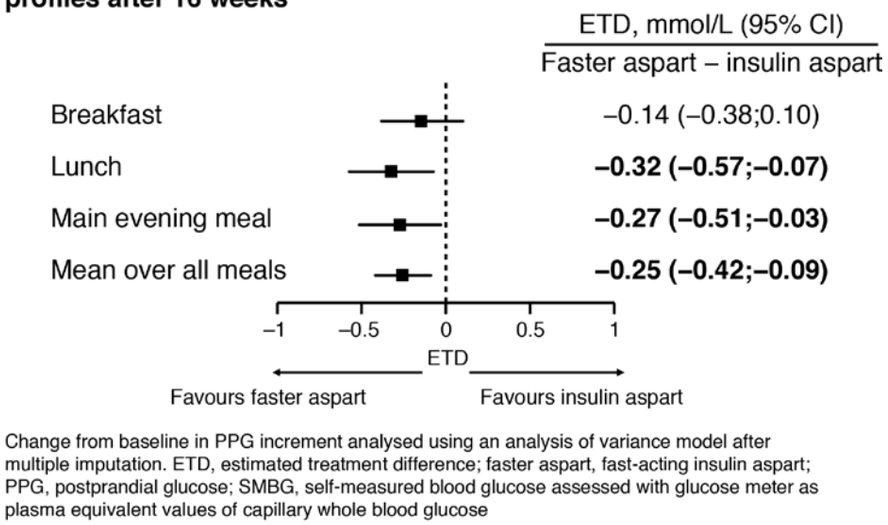
Background and aims: Fast-acting insulin aspart (faster aspart) is a mealtime insulin with more rapid absorption and greater early glucose-lowering effect than insulin aspart (IAsp). The aim of this trial (onset 9) was to evaluate the efficacy and safety of faster aspart compared with IAsp, both with insulin degludec with or without metformin, in adults with advanced type 2 diabetes (T2D) not optimally controlled with a basal-bolus regimen.

Materials and methods: This was a 16-week, multicentre, double-blind, treat-to-target trial. Following a 12-week run-in period to optimise basal insulin, participants were randomised (1:1) to mealtime faster aspart (n=546) or IAsp (n=545), both with insulin degludec. All available information regardless of treatment discontinuation or use of ancillary treatment was used for evaluation of effect.

Results: Non-inferiority (0.4% margin) with regard to change from baseline in HbA_{1c} 16 weeks after randomisation (primary endpoint) was confirmed for faster aspart vs. IAsp (estimated treatment difference [ETD] [95% CI] –0.04% [–0.11;0.03]; –0.39 mmol/mol [–1.15;0.37]). Faster aspart was superior to IAsp for change from baseline in 1-h postprandial glucose (PPG) increment using a meal test (ETD [95% CI] –0.40 mmol/L [–0.66;–0.14]; –7.23 mg/dL [–11.92;–2.55]). Change from baseline in 1-h PPG increment based on self-measured blood glucose profiles was statistically in favour of faster aspart after lunch, the main evening meal and over all meals (**Figure**). Change from baseline in 1,5-anhydroglucitol also favoured faster aspart over IAsp (ETD [95% CI] 0.50 ug/mL [0.11;0.89]). The overall rate of treatment-emergent severe or blood glucose (BG)-confirmed (plasma glucose equivalent <3.1 mmol/L [56 mg/dL]) hypoglycaemia was statistically significantly lower for faster aspart vs. IAsp (estimated treatment ratio [ETR] [95% CI] 0.81 [0.68;0.97]), as was the rate within 4 h after a meal (ETR [95% CI] 0.78 [0.63;0.98]). Adverse event profiles were similar between treatments.

Conclusion: In combination with insulin degludec, faster aspart provided effective overall glycaemic control, superior PPG control and a lower rate of severe or BG-confirmed hypoglycaemia vs. IAsp in adults with advanced T2D not optimally controlled with a basal-bolus regimen.

Figure. Change from baseline in 1-h PPG increment from SMBG profiles after 16 weeks



Change from baseline in PPG increment analysed using an analysis of variance model after multiple imputation. ETD, estimated treatment difference; faster aspart, fast-acting insulin aspart; PPG, postprandial glucose; SMBG, self-measured blood glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose

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