

A randomized, multicenter trial evaluating the efficacy and safety of fast-acting insulin aspart in continuous subcutaneous insulin infusion in adults with type 1 diabetes (ONSET 5)

Background

- Only about 30% of adults with Type 1 Diabetes using continuous subcutaneous insulin infusion devices achieve Hemoglobin A1c levels of less than 7.0%.
- There is a need for better therapeutic interventions for more with Type 1 diabetes (e.g. newer drugs, more effective regimens, etc.)

Objective

- To demonstrate the non-inferiority of fast-acting insulin aspart compared to (normal/regular) insulin aspart when used in continuous subcutaneous insulin infusion in patients with Type 1 diabetes.

Methods

- This was a double-blind, treat-to-target, randomized, 16-week, intention-to-treat trial comparing continuous subcutaneous insulin infusion of “faster aspart” (n = 236) to insulin aspart (n = 236).

Results

- At a margin of 0.4% or less, faster aspart was non-inferior to Insulin aspart regarding the change from baseline in hemoglobin A1c (primary endpoint).
- The mean hemoglobin A1c changed from 7.49% at baseline to 7.44% with faster aspart and to 7.35% with Insulin aspart after 16 weeks of treatment, with an estimated treatment difference of 0.09% (95% CI 0.01; 0.17; P < 0.001) for non-inferiority (0.4% margin; P < 0.02 for statistical significance in favor of Insulin aspart).
- Faster aspart was superior to Insulin aspart in change from baseline in 1-hour postprandial glucose (PPG) after a standardized meal test (−16.4 mg/dL [95% CI −25.7; −7.0]; P = 0.001). There were statistically significant reductions at 30 minutes and 2 hours and no statistically significant reductions at 3 and 4 hours.
- The improvement in 1 hour PPG from baseline after all meals was −7.69 mg/dL (95% CI −12.15; −3.23).
- There was no statistically significant difference in the overall rate of severe or blood glucose- confirmed hypoglycemia (estimated rate ratio 1.00 [95% CI 0.85; 1.16]).
- The rate of Blood Glucose confirmed hypoglycemic episodes 1 hour after meals was significantly higher in Faster aspart than Insulin aspart.

- A numerical difference in severe hypoglycemic episodes between faster aspart and Insulin aspart was seen in the treatment (21 vs 7) and 4-week run-in periods (4 vs 0).

Strengths

- The study was Multinational and therefore had the potential for wide-ranging population applicability.
- It was randomized, double-blinded and had a large/adequate study population (called for 450 and 476 were randomized.)

Limitations

- The study was funded by the drug company that makes fast acting insulin aspart. Authors were affiliated with the drug company.
- The study excluded patients with eGFRs less than 60. The study excluded children.
- An analysis of children might've been useful since type 1 diabetes often begins in childhood.
- The study doesn't ultimately demonstrate any positive net risk/benefit of fast aspart over regular aspart.

Conclusion

- Faster aspart is not anymore efficacious in terms of A1c reduction than regular aspart with higher levels of hypoglycemia. There doesn't seem to be any benefit over risk. Both drugs are the same price. There doesn't appear to be a clinical or economical benefit to this formulation, at least for this indication.

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