EXPLORATORY EVALUATION OF TECHNOSPHERE INSULIN WITH AUTOMATED INSULIN DELIVERY: IMPACT OF TOTAL DAILY DOSE ALGORITHMS

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OBJECTIVE

To assess the interaction between inhaled insulin use and automated insulin delivery (AID) algorithm design, with emphasis on algorithms that adapt insulin delivery based on total daily dose

CONCLUSIONS

- Integrating inhaled insulin into an AID system may differ across algorithms.
- Algorithms that do not adapt insulin delivery based on total daily dose may respond differently to insulin delivered outside the pump.
- Future AID evaluation should consider accounting for exogenous insulin, such as inhaled insulin, to support broader therapeutic interoperability.

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INTRODUCTION

Inhaled insulin (Technosphere® insulin, TI, Afrezza) is a dry powder consisting of microscopic carrier particles onto which recombinant human insulin is adsorbed.

Inhaled insulin is used for prandial and correction dosing and has a rapid pharmacokinetic profile that more closely approximates physiologic postprandial insulin exposure compared with subcutaneous rapid-acting analogs.

AID systems differ in their adaptive logic, including whether insulin delivery is recalibrated using recent total daily dose (TDD). Insulin delivered outside the pump is not captured in pump-based metrics (e.g., insulin-on-board), which may affect algorithms designed to adapt based on TDD.

- **TDD-dependent algorithms:** Use recent pump-recorded TDD to adapt basal delivery and correction dosing behavior. Insulin delivered outside the pump reduces apparent TDD, which may alter correction aggressiveness and slow algorithm recalibration.

- **TDD-independent algorithms:** Rely primarily on programmed parameters and real-time continuous glucose monitoring (CGM) feedback, with minimal dependence on cumulative daily insulin delivery. These systems may be less sensitive to unrecorded prandial insulin administered outside the pump.

METHODS

The Afrezza with Basal Combination study was a randomized controlled trial in adults with type 1 diabetes using commercially available AID systems. Participants were randomized to one of three treatment arms:

1. Continued use of their existing AID system
2. Transition from AID to inhaled insulin for meals and corrections plus once-daily basal insulin degludec
3. Use of inhaled insulin for meals and corrections while continuing AID for basal insulin delivery

This analysis includes participants randomized to inhaled insulin with AID, stratified by AID algorithm (TDD-dependent vs. TDD-independent).

Outcomes in this descriptive analysis included change in hemoglobin A1c (HbA1c) from baseline to Day 90 and CGM-derived time in range (70–180 mg/dL). Formal hypothesis testing was not performed due to limited sample size.

RESULTS

Of the nine participants who used inhaled insulin with AID providing basal insulin only, six used TDD-dependent algorithms and three used TDD-independent algorithms.

After 90 days, mean reduction in HbA1c was numerically greater with TDD-independent algorithms (-0.33%) compared to the TDD-dependent algorithms (-0.22%), **Figure 1**. An improvement in the mean CGM time in range (TIR) from baseline to end of study was observed in the TDD-independent group, **Figure 2**.

Table 1. Baseline Characteristics

	TDD-Dependent N=6	TDD-Independent N=3
Mean Age, yrs (SD)	49.9 (12.6)	42.5 (15.2)
Mean Diabetes Duration, yrs (SD)	36.2 (17.3)	17.0 (21.7)
Female, n (%)	3 (50)	3 (100)
Mean HbA1c (SD)	7.95 (0.94)	7.57 (0.15)

Figure 1. Change in HbA1c (Day 90)

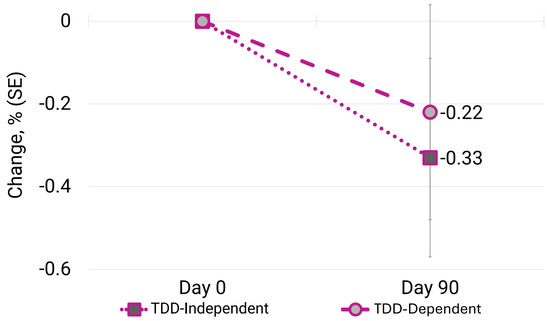

Figure 2. Mean Time in Range 70-180 mg/dL