INHALED INSULIN DEMONSTRATES LOWER VARIABILITY AND FASTER ONSET COMPARED TO SUBCUTANEOUS RAPID ACTING ANALOGS

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OBJECTIVE

To characterize postprandial glucose excursion by weight-normalized prandial dose (U/kg) for inhaled insulin versus subcutaneous rapid-acting analogs (RAA) during a standardized meal challenge

CONCLUSIONS

- Participants in the higher U/kg inhaled insulin stratum demonstrated lower mean glucose excursion than the higher U/kg RAA stratum ($p<0.05$).
- RAA strata (low vs high U/kg) did not show a statistically different excursion pattern, whereas inhaled insulin showed a low vs high separation ($p<0.05$) supporting further evaluation of weight-normalized dose optimization strategies.

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INTRODUCTION

Postprandial glucose management in type 1 diabetes is influenced by insulin pharmacodynamics, meal composition, and individual insulin sensitivity. Subcutaneous rapid-acting analogs (RAA) are commonly dosed and interpreted in relation to body size, and weight-normalized units (U/kg) are frequently used to contextualize insulin needs across individuals.

Inhaled Technosphere® insulin is an ultra rapid-acting prandial insulin delivered via pulmonary administration, producing a time-action profile that differs from subcutaneous RAA. Because the route of administration and absorption kinetics differ from subcutaneous injection, a simple unit-to-unit conversion from RAA does not result in equivalent postprandial glucose coverage, and the relationship between U/kg and glycemic response differs for inhaled insulin compared with RAA.

METHODS

INHALE-3 was a phase 4, multi-center, 17-week randomized controlled trial evaluating efficacy and safety of inhaled insulin combined with insulin degludec versus usual care (UC) in adults ≥18 years with type 1 diabetes.

Participants randomized to inhaled insulin completed two standardized 120-minute meal challenges (initial conversion dose from their typical RAA dose and post-titration at Week 17). UC participants completed the same meal challenge at baseline using their RAA regimen. Glucose excursion was measured as glucose change from baseline. All standard meals were BOOST shakes (37 g of carbohydrates).

Meal challenge insulin dose was divided by body weight (kg) at the time of dose. Due to unit-to-unit differences between inhaled insulin and RAA and differing dose distributions, doses were categorized within treatment into:

- Low: ≤ median U/kg
- High: > median U/kg

For inhaled insulin, the median split was based on the titrated meal challenge (Week 17) distribution, reflecting individualized dosing after titration rather than initial conversion dosing.

Mean glucose excursion was compared within and between strata using two-sample t-tests at each meal challenge timepoint.

RESULTS

Analyses included 61 UC and 161 inhaled insulin meal challenges, **Table 1**.

Table 1. Baseline Characteristics for Randomized Participants

	Inhaled Insulin N=61	UC N=61
Mean Age, yrs (SD)	45.9 (14.2)	44.7 (16.3)
Female, n (%)	33 (54.1)	32 (52.5)
Mean HbA1c (SD)	7.58 (1.0)	7.59 (0.8)
Mean BMI (SD)	27.8 (4.5)	28.2 (5.5)

Among the 61 participants randomized to inhaled insulin, all completed the first-dose meal challenge and 49 completed the Week 17 optimized meal challenge. Among the 61 participants randomized to UC, 51 completed the inhaled insulin first-dose meal challenge at Week 17. In total, 161 inhaled insulin meal challenges were conducted, including both first-dose and optimized-dose assessments.

Meal challenge doses were stratified into Low vs High U/kg using the UC median and the Week 17 inhaled insulin median. Within-group analyses showed no difference between UC-Low and UC-High, while inhaled insulin-High demonstrated lower glucose excursion than inhaled insulin-Low from 20–120 minutes ($p<0.05$; **Table 2**).

Between groups, inhaled insulin-High demonstrated lower mean glucose excursion than UC-High from 30–120 minutes ($p<0.05$; **Figure 1**), with no difference between Low U/kg groups **Figure 2**.

Safety

No new safety signals were identified.

Table 2. Mean U/Kg by Group Strata

Group	U/kg Strata (n)	Mean (SD)	Within-Group Glucose Excursion
UC	Low, n = 31	0.042 (0.009)	*No significant difference*
	High, n = 29	0.084 (0.048)	
	Total, n = 61	0.062 (0.040)	
Inhaled Insulin	Low, n = 89	0.074 (0.019)	*p<0.05 at timepoints t=20-120 min*
	High, n = 69	0.157 (0.056)	
	Total, n = 161	0.110 (0.057)	

Figure 1. High U/kg Strata Glucose Excursion

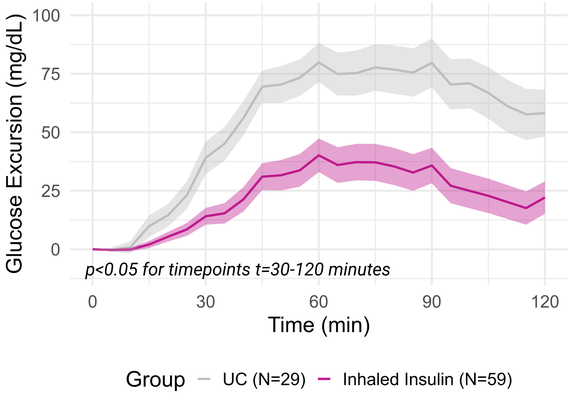

Figure 2. Low U/kg Strata Glucose Excursion