EFFICACY AND SAFETY OF INHALED INSULIN VERSUS RAPID-ACTING ANALOGS IN YOUTH WITH HBA1C ≤9.5%: SUBGROUP ANALYSIS FROM INHALE-1

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OBJECTIVE

To evaluate 26-week change in HbA1c among participants with baseline HbA1c ≤9.5% from the INHALE-1 study

CONCLUSIONS

- In youth with baseline HbA1c ≤9.5%, inhaled insulin achieved non-inferior glycemic outcomes compared with rapid-acting analog (RAA) insulins after 26 weeks.
- Higher baseline HbA1c ranges may be associated with increased response variability and adaptation to therapy.
- When considering therapy options, it's essential to align treatment with the patient's preferences, readiness, and goals.

INTRODUCTION

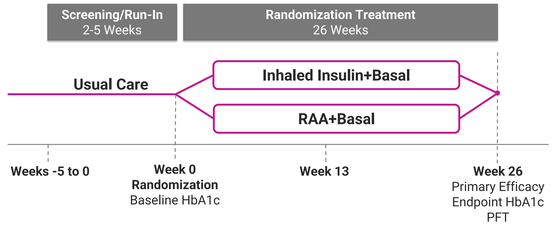
Inhaled insulin (Technosphere® insulin, TI) is a dry powder consisting of microscopic carrier particles onto which recombinant human insulin is adsorbed.

This subgroup analysis evaluates the safety and efficacy of inhaled insulin in pediatric participants from INHALE-1. The original study design included participants across a broad baseline HbA1c range (7.0-11.0%) to support generalizability across pediatric glycemic profiles. This analysis focuses on participants with a baseline HbA1c ≤9.5%, a threshold commonly applied in pediatric prandial insulin trials to limit heterogeneity due to severe dysglycemia, barriers to medication taking, and insulin resistance, to better isolate prandial insulin effects on glycemic endpoints.

METHODS

INHALE-1 was a Phase 3, open-label, randomized study evaluating the efficacy and safety of inhaled insulin plus basal insulin versus RAA plus basal insulin in pediatric participants 4-17 years of age with type 1 (T1D) or 2 (T2D) diabetes mellitus, **Figure 1**.

Figure 1. INHALE-1 Study Design



Participants were randomized and received 26 weeks of treatment. The primary endpoint assessed non-inferior change in HbA1c between groups from baseline to Week 26, upper 95% confidence interval (CI) margin of 0.4%, which was not met in the intent-to-treat population. This analysis selected participants with baseline HbA1c ≤9.5%.

HbA1c change was analyzed using an ANCOVA model adjusted for treatment, diabetes type, age, and baseline HbA1c.

Missing post-baseline values were imputed using a return-to-baseline approach.

Inclusion Criteria

- Age 4 to <18 years
- T1D on insulin for 6 months, or T2D on insulin for 3 months
- Multiple daily injections for at least 2 weeks
- At least 2 units RAA per meal
- Continuous glucose monitor (CGM) use ≥70% over 2 weeks
- FEV_1 or FEV_1/forced vital capacity >80% of percent predicted

RESULTS

The INHALE-1 study enrolled 230 participants (117 in the inhaled insulin group and 113 in the RAA group). Of these, 209 participants had a baseline HbA1c ≤9.5%, with 106 in the inhaled insulin group and 103 in the RAA group, maintaining expected sample size of 100 or more participants per arm, **Table 1**.

Table 1. Baseline Characteristics

	Inhaled Insulin N=106	RAA N=103
Mean Age, yrs (SD)	12.7 (2.9)	12.6 (3.1)
Female, n (%)	37 (34.9)	39 (37.9)
Mean HbA1c (SD)	8.03 (0.7)	8.02 (0.8)

At Week 26, least square (LS) mean HbA1c change was 0.19% with inhaled insulin and 0.08% with RAA, **Table 2**. The LS mean between-group difference was 0.11% (95% CI: -0.145, 0.364), meeting the prespecified non-inferiority criterion (upper CI <0.4%), **Figure 2.**

Table 2. HbA1c Change from Baseline to Week 26

	LS Mean (SE)	95% CI
Inhaled Insulin N=106	0.19 (0.09)	(0.007, 0.365)
RAA N=103	0.08 (0.09)	(-0.103, 0.256)

Figure 2. HbA1c, Baseline and Week 26

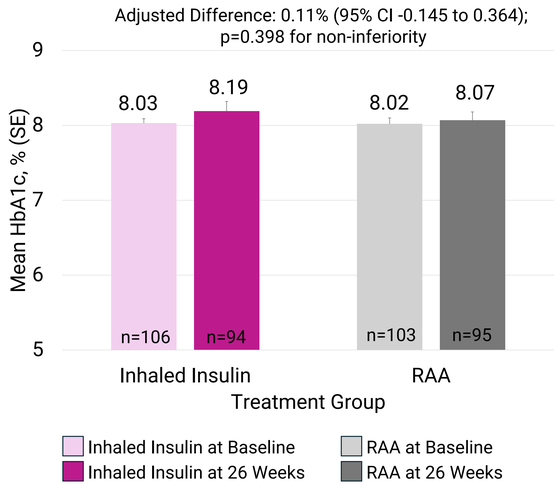
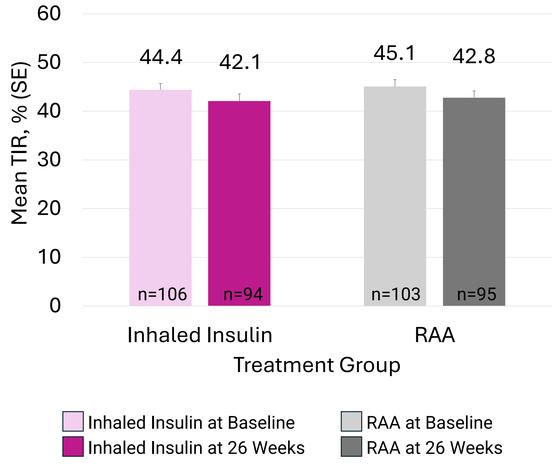


Figure 3. Time in Range (TIR), Baseline and Week 26



Mean time in range values at baseline and Week 26 were comparable between treatment groups, **Figure 3**.

Safety

There were no new safety signals and similar rates of adverse events compared to adult data.

Association of Diabetes Care and Education Specialists · August 7-10, 2026 · Columbus, OH, USA

Original Presentation: "Efficacy and Safety of Inhaled Insulin versus Rapid-Acting Analogs in Youth with HbA1c ≤9.5%: Subgroup Analysis from INHALE-1" presented at ADA 2026, New Orleans, LA, USA by Kevin Kaiserman, MD