INHALED INSULIN DEMONSTRATES LESS WEIGHT GAIN AND MORE FAVORABLE BMI PERCENTILE CHANGES THAN RAPID-ACTING INSULIN ANALOGS IN YOUTH WITH DIABETES

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OBJECTIVE

To evaluate change in weight and body mass index (BMI) percentile between inhaled insulin and rapid-acting insulin analog (RAA) youth cohorts in the INHALE-1 study

CONCLUSIONS

- In youth, inhaled insulin was associated with less weight gain and more favorable BMI percentile outcomes than RAA after 26 weeks
- More pronounced treatment effects were observed among early adolescents and female participants
- Inhaled insulin may be a valuable treatment option considering weight-related treatment burden in diabetes care

INTRODUCTION

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

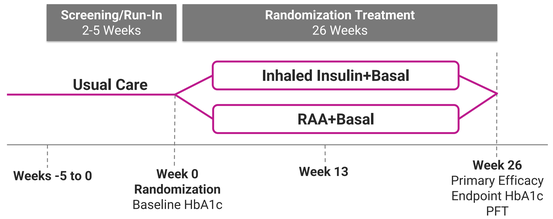
Weight gain is a clinically important challenge and common concern associated with injectable insulin therapy in youth with diabetes, which may affect long-term cardiometabolic health and treatment adherence.

This post hoc analysis of the Phase 3 INHALE-1 trial evaluated changes in weight and BMI percentile following 26 weeks of treatment with inhaled insulin compared to RAA treatment in pediatric participants stratified by age and sex.

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 or 2 type 2 diabetes mellitus, **Figure 1.**

Figure 1. INHALE-1 Study Design



Participants were randomized and received 26 weeks of treatment. The primary endpoint assessed change in HbA1c between groups from baseline to Week 26, upper 95% confidence interval (CI) and noninferiority margin of 0.4%.

Post-hoc descriptive analyses evaluated the change from Baseline to Week 26 in weight and BMI percentile. Demographic subgroups by age (4-10, 11-13, and 14-17 years) and sex were evaluated. Between-group comparisons were conducted using a two-sample, two-sided t-test.

RESULTS

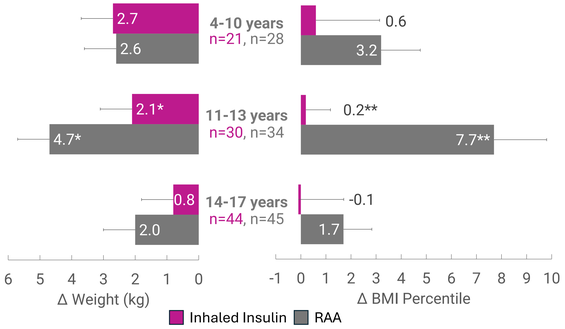
The INHALE-1 study enrolled 230 participants (117 in the inhaled insulin group and 113 in the RAA group). Of these, there were non-missing baseline and Week 26 weight and BMI percentile measurements for 95 participants in the inhaled insulin group and 107 in the RAA group, **Table 1**.

Table 1. Baseline Characteristics

	Inhaled Insulin N=95	RAA N=107
Mean Age, yrs (SD)	12.8 (3.0)	12.3 (3.1)
Female, n (%)	33 (34.7)	40 (37.4)
Mean HbA1c, % (SD)	8.2 (0.9)	8.2 (1.0)

Participants receiving inhaled insulin demonstrated lower weight gain and BMI percentile change compared with RAA, **Figure 2**. Participants aged 4-10 years and 14-17 years demonstrated numerically lower weight and BMI percentile outcomes with inhaled insulin. The most pronounced treatment effects were observed among early adolescents aged 11-13 years.

Figure 2. Weight and BMI Percentile Change After 26 Weeks by Age Cohort



*between-group difference -2.6 kg, p<0.01; **between-group difference -7.5, p<0.01

Among participants aged 11-13 years, both female and male patients experienced reduced weight gain compared with RAA, **Figure 3**, while males demonstrated greater improvement in BMI percentile outcomes, **Figure 4**.

Figure 3. Change in Weight by Sex in Participants Aged 11-13 Years from Baseline to 26 Weeks

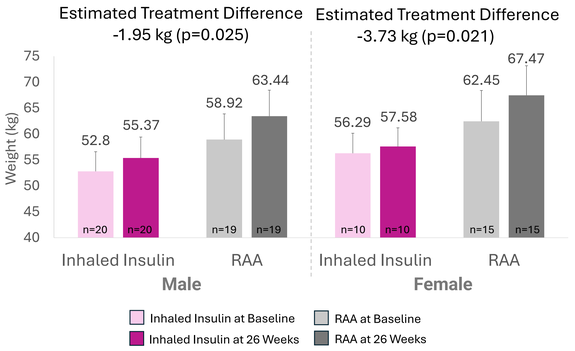
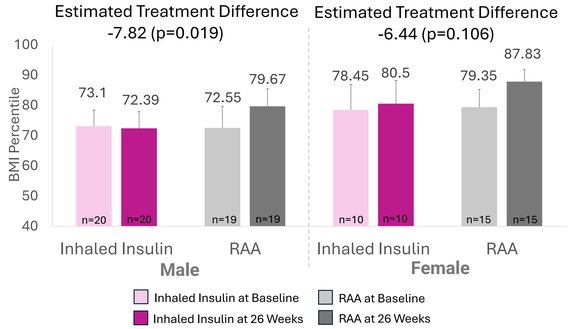


Figure 4. Change in BMI Percentile by Sex in Participants Aged 11-13 Years from Baseline to 26 Weeks



Across all ages, females treated with inhaled insulin demonstrated less weight gain (treatment difference: -2.417 kg, p=0.003) and lower BMI percentile change (treatment difference: -4.727 points, p=0.035) compared with females receiving RAA. Similarly, males across all ages treated with inhaled insulin demonstrated numerically less weight gain and lower BMI percentile change than those receiving RAA, however the difference did not reach statistical significance (p>0.05).

Safety

No new safety signals were identified, and there was no clinically meaningful impact on pulmonary function over a 26-week period.

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