

# INHALE-1: A 26-week Primary Treatment with 26-week Extension, Open-label, Randomized Clinical Trial Evaluating the Efficacy and Safety of Afrezza® vs Rapid-Acting Analogue Insulin in Pediatric Subjects with Diabetes



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## OBJECTIVE

To evaluate the efficacy and safety of inhaled Technosphere® Insulin (TI) versus rapid acting analog (RAA) insulin in pediatric diabetes.

## INTRODUCTION

Inhaled Technosphere® Insulin (TI) has an ultra-rapid acting profile, due to its unique pharmacokinetic and pharmacodynamic properties, resulting in a much faster time-to-peak effect and clearance compared to subcutaneously (SC) administered RAA.

Most youth with diabetes do not achieve glycemic goals. Due to TI's profile, it has the potential to enhance flexibility of insulin dosing and improve outcomes.

TI is approved for use in adults in USA, India, and Brazil and is available in three color-coded dosage cartridges: 4, 8, and 12 "Afrezza" units. To achieve higher doses than 12 Afrezza units, multiple cartridges are inhaled.

The bioequivalent TI dose in units is 2-3X the RAA dose.

## METHODS

INHALE-1 included a 26-week randomized trial (RCT) followed by a 26-week extension phase (EXT), conducted at 38 sites in the U.S. between September 2021 and March 2025.

### Eligibility Criteria

- Age 4 to <18 years
- T1D or T2D clinical diagnosis
- Used insulin for ≥6 months for T1D or ≥3 months for T2D
- Treated with MDI for at least 2 weeks
- HbA1c ≥7.0% and ≤11.0%
- At least 2 units RAA per meal
- FEV1 or FEV1/FVC >80% of predicted GLI value

RCT: Randomized assignment to TI or RAA to use in addition to basal insulin. Both groups used real-time CGM (Dexcom G6).

- Primary outcome: change in HbA1c at 26w, tested for non-inferiority (margin 0.4%)

EXT: Both groups used TI + basal insulin.

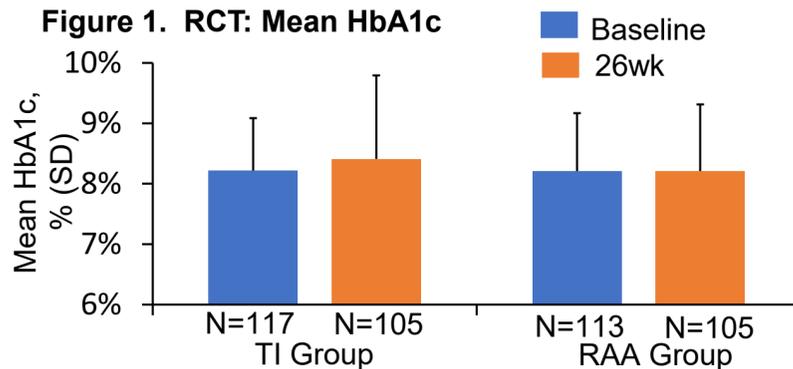
## ACKNOWLEDGEMENTS

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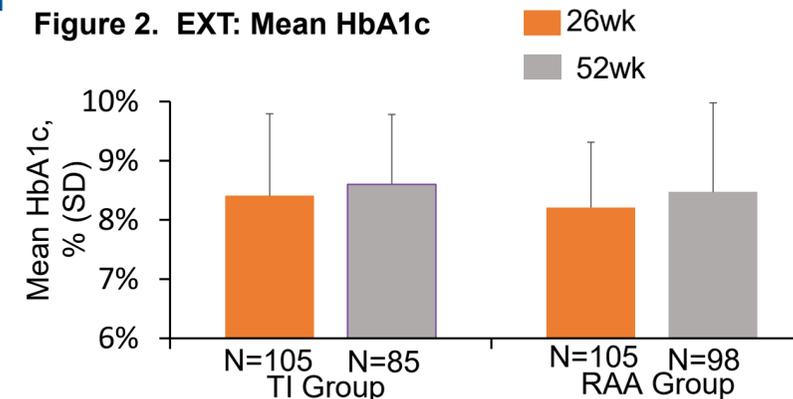
## RESULTS

### Participant Characteristics

- Mean age 12.6yrs (range 4-17 yrs)
- 38% female, 77% White, 20% Hispanic
- 98% T1D, 2% T2D. Mean duration 4.5 yrs

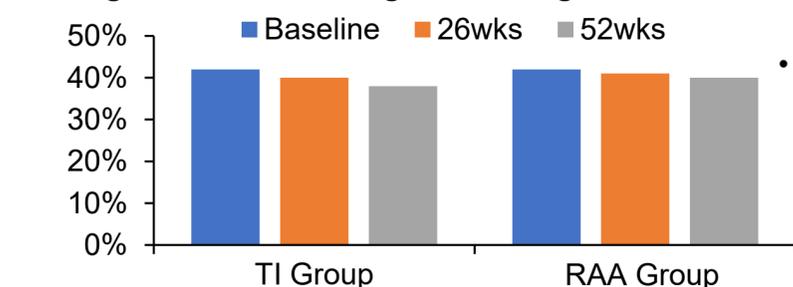


- RCT Treatment Group Difference (95% CI) pvalue for non-inferiority- 0.4% margin
  - ITT: 0.18% (-0.07 to 0.43) 0.091
  - Sensitivity Analysis: 0.14% (-0.10 to 0.37) 0.026



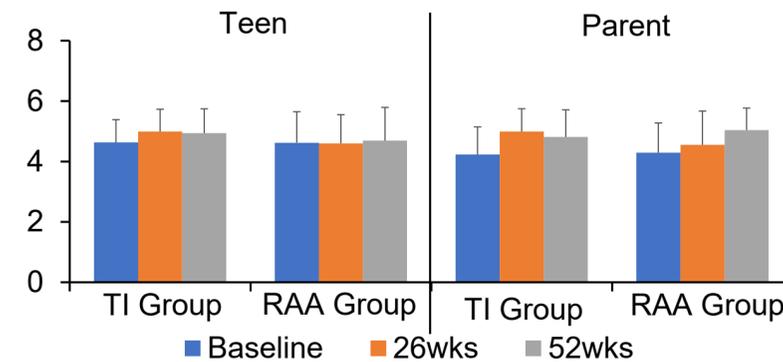
- EXT: Both groups with slightly higher HbA1c at 52w compared with 26w

### Figure 3. Time in Range 70-180 mg/dL



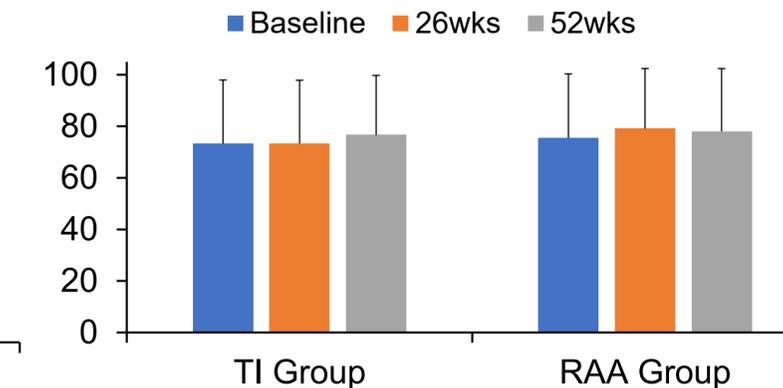
- Little change in TIR in both groups throughout RCT and EXT

### Figure 4. Treatment Satisfaction (DTSQ)



- RCT: greater treatment satisfaction with TI vs. RAA pooling Teens and Parents (p=0.004)
- EXT: treatment satisfaction appeared higher in Parents but not Teens after switching from RAA to TI

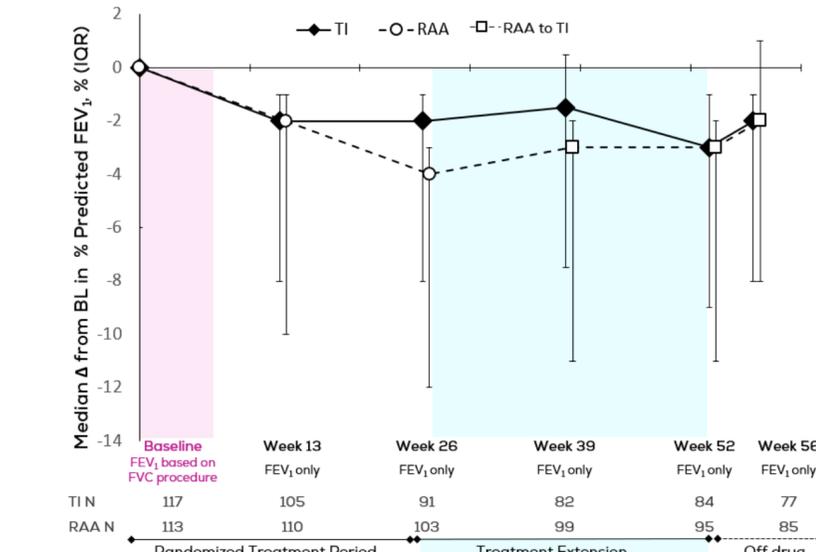
### Figure 5. BMI Percentile



- RCT: less weight gain and BMI increase with TI vs. RAA (p=0.009)
- EXT: BMI changes similar in both groups

## SAFETY

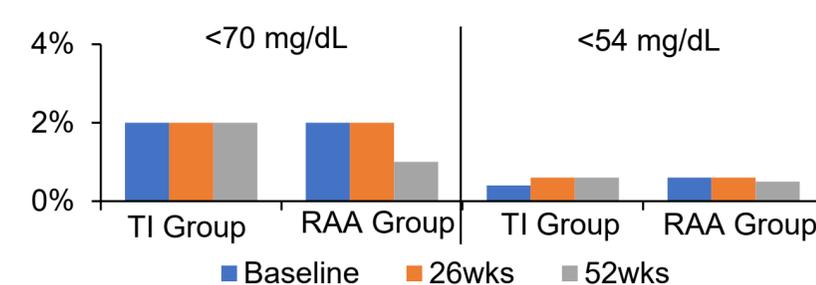
### Figure 6. Change from Baseline in Percent Predicted FEV1



### Change in FEV1

- RCT: similar with TI (-3.2%) and RAA (-3.9%) (p=0.54)
- EXT: similar comparing TI from baseline to 52wks RAA baseline to 52wks (-3.6%) (p=0.54)

### Figure 7. Percent Time <70 and <54 mg/dL



- Low levels of hypo throughout in both groups

## CONCLUSION

Inhaled Technosphere Insulin use by youth with diabetes is safe, associated with greater treatment satisfaction and less weight gain than RAA, and should be considered as an alternative to RAA in pediatric diabetes care.