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UNIVERSITY  
HEALTH

# INHALE-3

## A Randomized Trial Comparing Inhaled Insulin (Afrezza®) Plus Insulin Degludec Versus Usual Care Insulin Delivery in Adults with Type 1 Diabetes

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### Objective

To assess efficacy and safety of Technosphere® Insulin (TI) compared to usual care rapid acting insulin analogue (RAA) therapy comprising Automated Insulin Delivery (AID), Non-Automated Pumps, and Multiple Daily Injections (MDI) in patients with Type 1 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.

A significant proportion of individuals with type 1 diabetes are not achieving their glycemic targets including those on AID with SC RAA infusion<sup>1</sup>.

INHALE-3 is a 17-week randomized controlled trial comparing efficacy and safety of TI combined with insulin degludec versus usual care (AID, nonautomated pump, or MDI) in adult subjects with T1D. TI is approved for use in adults with diabetes and is available in three color-coded dosage cartridges: 4U (blue), 8U (green), and 12U (yellow)<sup>2</sup>.

### Methods

#### Study Population

Participants ≥18 years of age with T1D on either AID, MDI, or non-automated pumps (usual care) were enrolled.

#### Study Design

Participants were randomized one-to-one to TI plus degludec or continuation of their usual care for a seventeen week period.

Participants randomized to TI transitioned from their usual care therapy to TI for meals and corrections; and insulin degludec for daily long-acting insulin. Participants in the TI group used Dexcom G7 (Dexcom, San Diego, CA). The first dose of TI was performed in-clinic. TI participants converted from their RAA therapy using a modified dose conversion shown in Table 1, which is higher than in the United States Prescribing Information<sup>2</sup>. Participants in the usual care group remained on their insulin modality and continued use of their personal CGM. Prior to randomization and prior to week 17, participants from both groups wore a blinded G6 Pro (Dexcom, San Diego, CA) in addition to their real-time CGM for glucose measurements.

**Table 1. TI Dose Conversion**

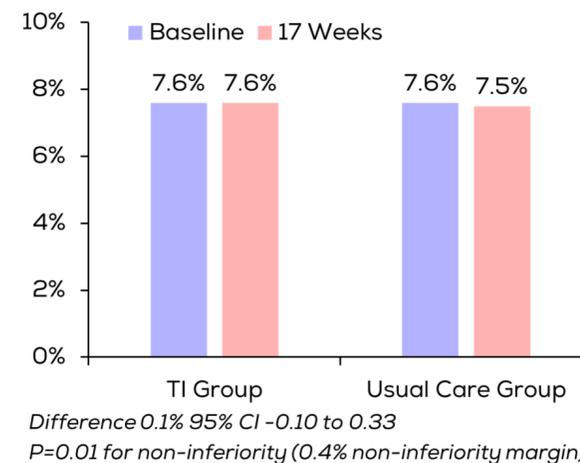
Injected Mealtime Insulin Dose (RAA)	Converted Inhaled Insulin Dose (TI)
≤3 units	4 units
4-5 units	8 units
6-7 units	12 units
8-9 units	16 units
10-11 units	20 units
≥12 units	24 units

### Results

Of the 123 randomized participants, 62 were assigned to TI group and 61 to usual care.

Primary endpoint of HbA1c was significant for noninferiority (margin 0.4%) (Figure 1). More participants using TI achieved TIR >70%; there were subgroups of participants that improved and worsened by ≥10% (Figure 2). 24 hr mean CGM glucose is shown in Figure 3.

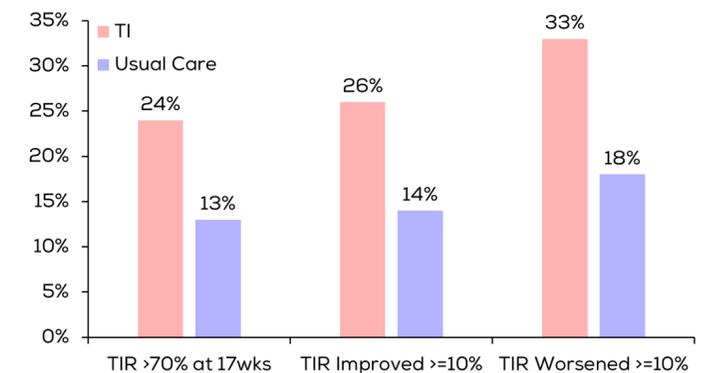
**Figure 1. HbA1c Results**



**Figure 2. CGM Time in Range (70-180 mg/dL)**



**Figure 3. 24-Hour CGM at 17 Weeks**



### Safety

One severe hypoglycemia event was reported in the TI group, which was adjudicated as not being related to TI. Two serious adverse events were reported in the UC group due to hospitalization: one for hyperglycemia/ketosis and one for appendectomy.

The most commonly reported adverse event in the TI group was cough, consistent with previous TI clinical trials. Cough was generally described as brief, at time of inhalation.

### Conclusions

- Study results support the use of inhaled TI combined with a long-acting basal insulin as an alternative to usual care, including MDI, non-automated pumps, and AID
- The study met its primary efficacy endpoint of a non-inferior change in HbA1c between baseline and week 17. While more subjects achieved time in range (TIR) >70% with TI, there were subgroups of patients using TI that had improvement and worsening of TIR by ≥10%