Post-Prandial Glucose Excursion with Inhaled Insulin versus Injected Insulin in Youth and Adults with Type 1 Diabetes

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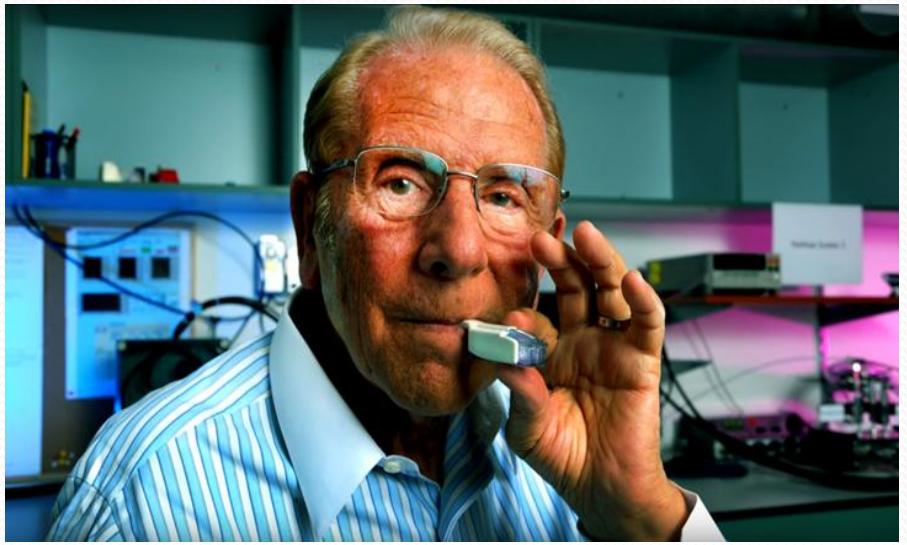
for the INHALE-1 Study Group

Conflict of Interests

- Consultant: MannKind, Sanofi, SAB Bio
- Scientific Advisory Board: SAB Bio

History of Technosphere Insulin (Afrezza®)

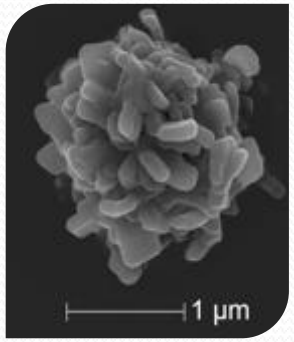
- In 1997, Al Mann saw the potential of a dry powder insulin formulation to achieve more rapid absorption into the blood stream than possible with SQ injections



- 20+ years to bring Technosphere Insulin (Afrezza®) to market
- Technosphere Insulin was approved by FDA in 2014
- Licensed to Sanofi in 2014 and returned to MannKind in 2016

Technosphere Insulin Inhaled Delivery

Technosphere
Microparticles (FDKP)



Water

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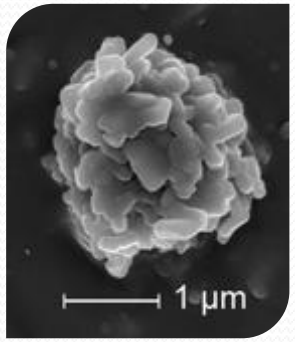
Human Regular Insulin

=

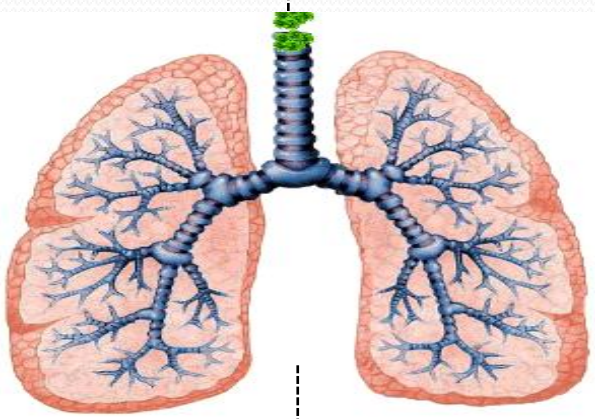
Technosphere Insulin (TI)



pH <6

Technosphere Insulin:
Insulin adsorption onto FDKP particle

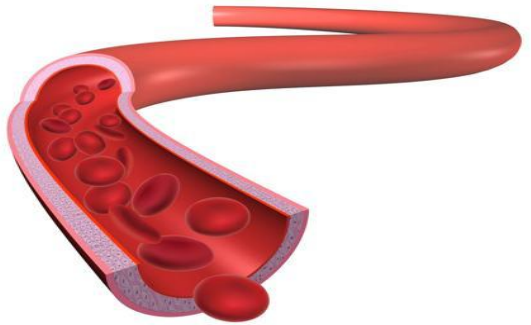
Bis-3,6(4-fumarylaminobutyl)-2,5-diketopiperazine (FDKP)



pH >6 (physiologic pH)

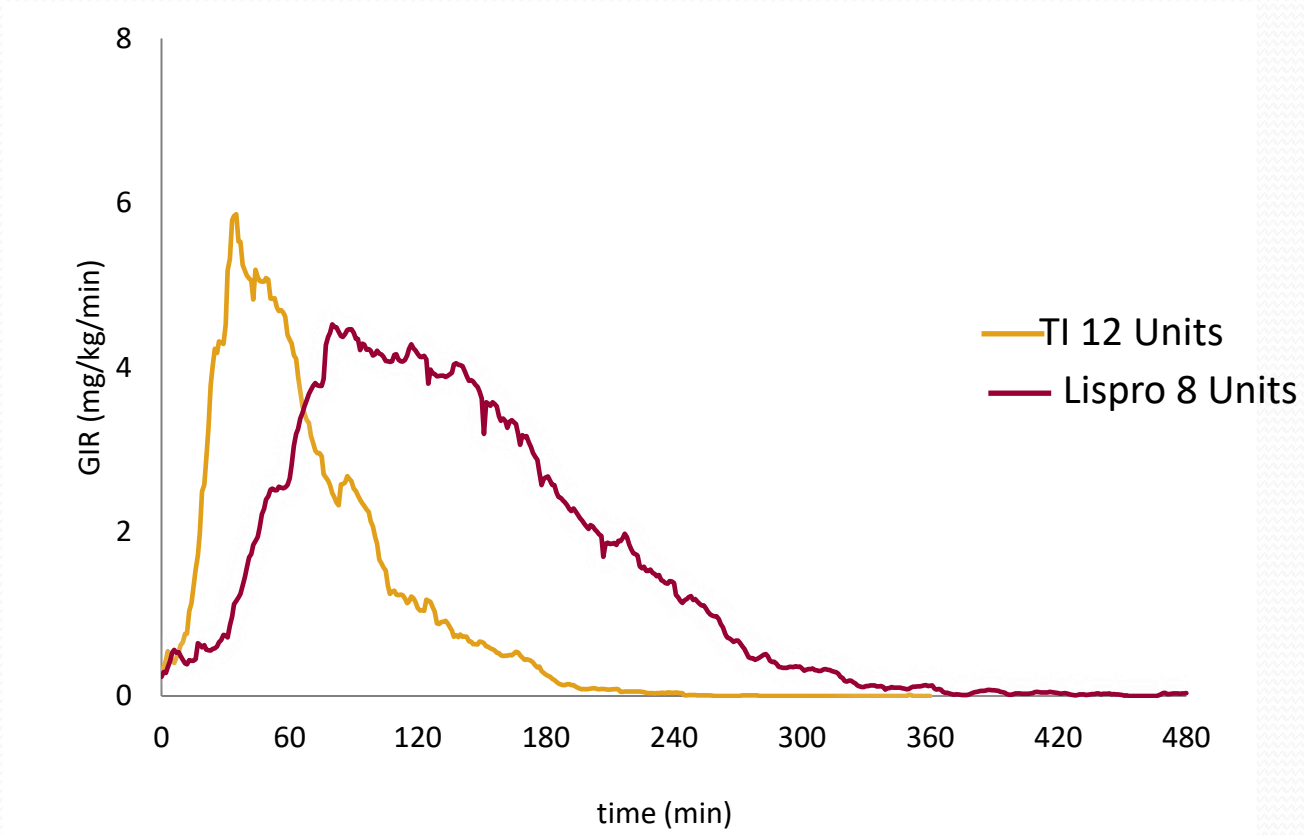
- Inhaled particles dissolve rapidly and separate
- FDKP and insulin are then quickly absorbed across the lung membrane

Blood Vessel



Insulin | FDKP

Pharmacodynamics of Technosphere Insulin Versus Rapid Acting Insulin Analogues



- TI maximum serum insulin concentration in 12-15min vs 45-60min for RAA
- TI effect dissipates faster than RAA potentially reducing post-meal hypoglycemia

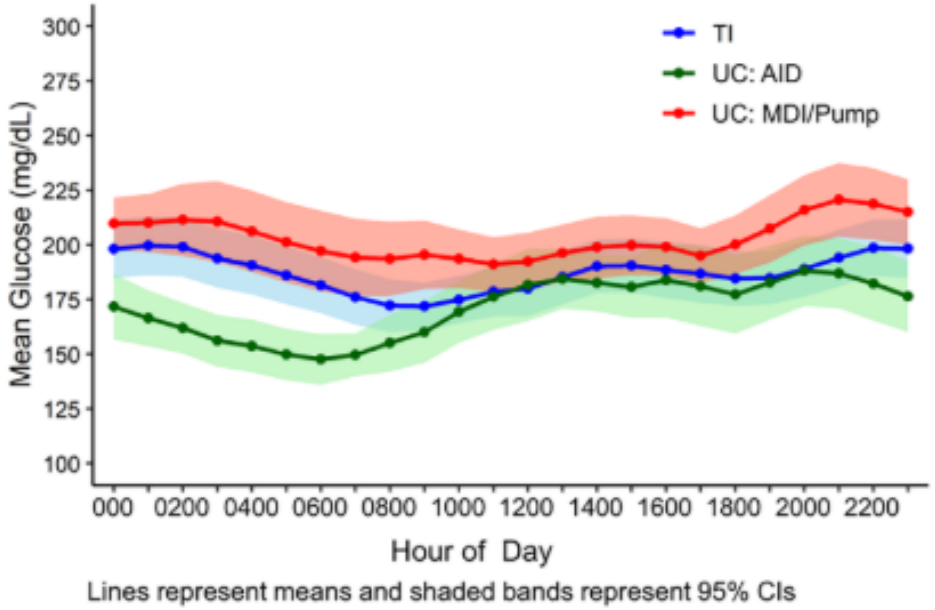
Background

- Inhaled Technosphere insulin (TI) has been shown to reduce post-prandial glucose excursions in adults with type 1 diabetes (T1D).

Results

Primary Outcome: Mean HbA_{1c}

	TI+Degludec (N=122)	Usual Care (N=121)
HbA_{1c}: baseline/17w	7.57%/7.62%	7.59%/7.54%
Trt group diff (95% CI)	0.11% (-0.10 to 0.33)	
P value (non inferiority)	0.01	



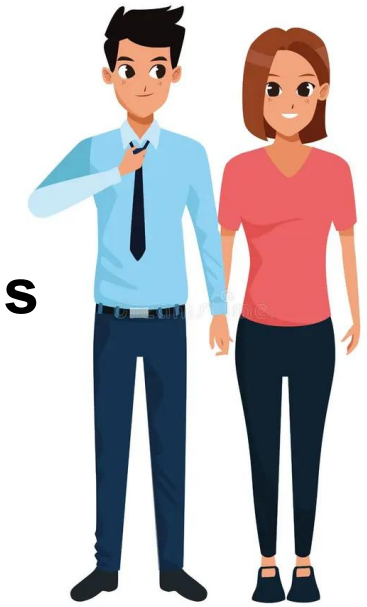
Lines represent means and shaded bands represent 95% CIs

INHALE-3 Study Group. A Randomized Trial Comparing Inhaled Insulin Plus Basal Insulin Versus Usual Care in Adults With Type 1 Diabetes. *Diabetes Care*. 2024

Background

- The aim of this study was to compare glucose excursions in youth using TI to bolus for a standardized meal with glucose excursions in adults using either TI or rapid acting analogue (RAA) insulin to bolus.

Versus



OR

Methods

INHALE-1 INHALE-3

- MDI insulin users with T1D in INHALE-1 (pediatrics) or INHALE-3 (adults)
- For the first dose of TI, an in-clinic meal challenge was performed with a standardized meal in 113 youth (6-<18 yrs) and 51 adults (22-77 yrs).
- Additionally, 26 adults had a meal challenge using RAA insulin.

- The TI dose was determined by rounding the usual RAA dose to the nearest whole number, multiplying by 2, and then rounding down to the nearest 4-unit dose of TI.

Methods

INHALE-3

Adult Meal Challenge

- Fasting; no bolus insulin for 4 hrs prior to start
- Glucose 91-219 mg/dL 15 min prior to start
- Boost (240 calories, 37g carbs, 10g protein, 4g fat)
- TI at start of meal or RAA 5-15 min prior to meal
- AID continued (TI group: Control-IQ in sleep mode)

RAA Dose	Inhaled Insulin Dose ("Afrezza Units")
≤3	4
4-5	8
6-7	12
8-9	16
10-11	20
≥12	24

Results

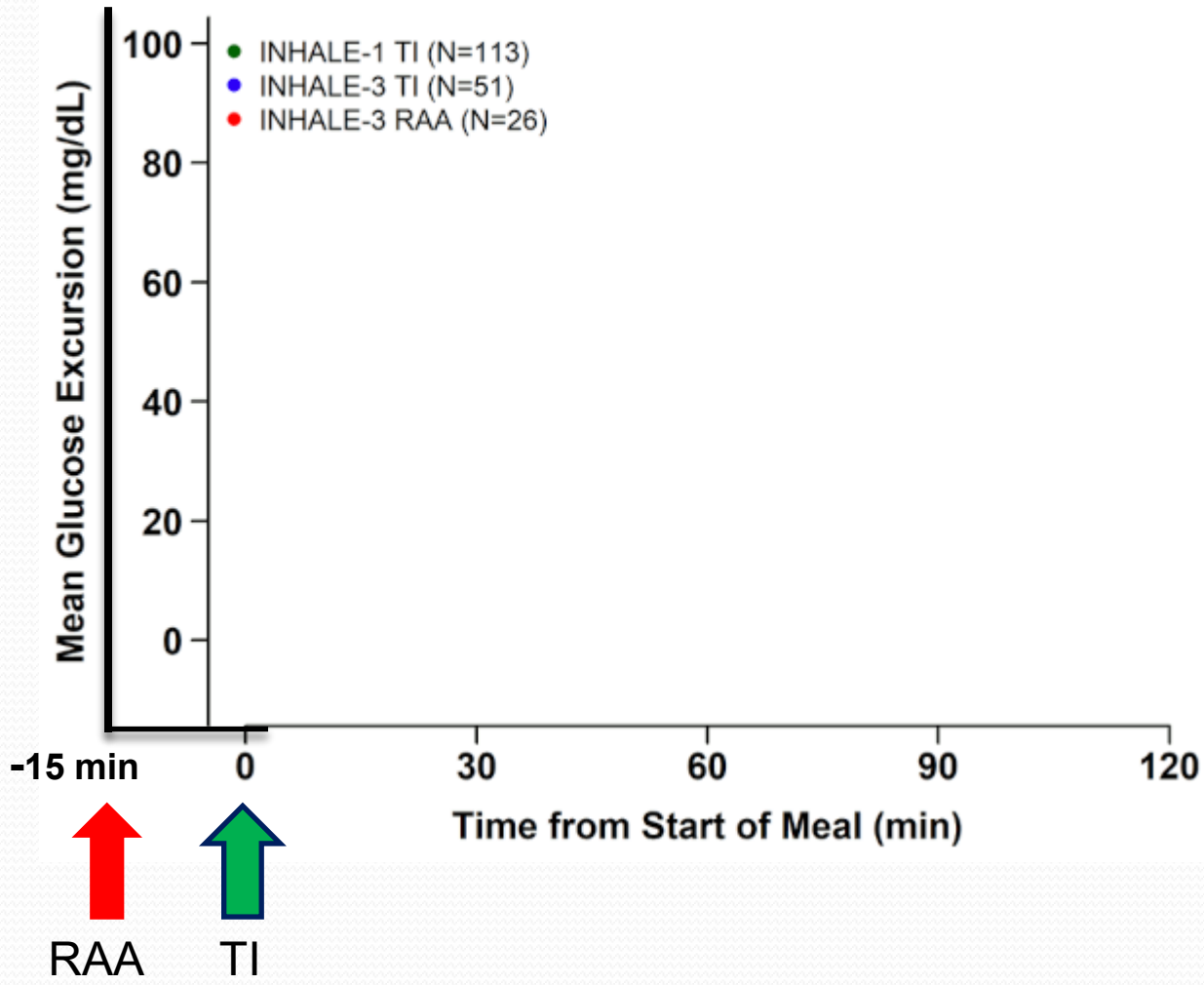
Inhaled Insulin to Rapid Analogue Ratio for First Meal

Pediatrics - Mean (SD)	1.9 (0.3)
Adults - Mean (SD)	1.8 (0.3)

Results

- Mean (±SD) glucose excursion less with TI
  - 69±56 mg/dL TI in youth
  - 73±50 mg/dL TI in adults
  - 101±45 mg/dL RAA in adults

- Time to peak glucose shorter with TI:
  - 69±34 min in youth with TI
  - 71±36 min in adults with TI
  - 78±31 min in adults with RAA



Summary

The post-prandial glucose excursion with TI appears similar in youth to that which has been reported in adults and is substantially lower than the excursion following a bolus with RAA insulin.

Primary Outcome INHALE-1

- Non-Inferiority of TI vs RAA
- To be reported at ADA 2025 (Chicago)

Funding

- Study support from MannKind

Investigators / Sites