Kinexum ADA 2022 report

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- It synthesizes selected data presented during the ADA 2022 conference, completed with publicly available data.
- It includes Sam's personal comments and opinions, underlined words are clickable links to other slides or external references.
- If you have comments, please contact Sam by email (samcollaudin@kinexum.com)
- Disclosure: Business strategy consultant at Kinexum, consultant for Modular Medical, CEO of Abvance Therapeutics, chairman of a non for-profit French health care insurance company (Groupe Uitsem).
- This report synthetizing external data, Sam cannot guarantee 100% accuracy of them.
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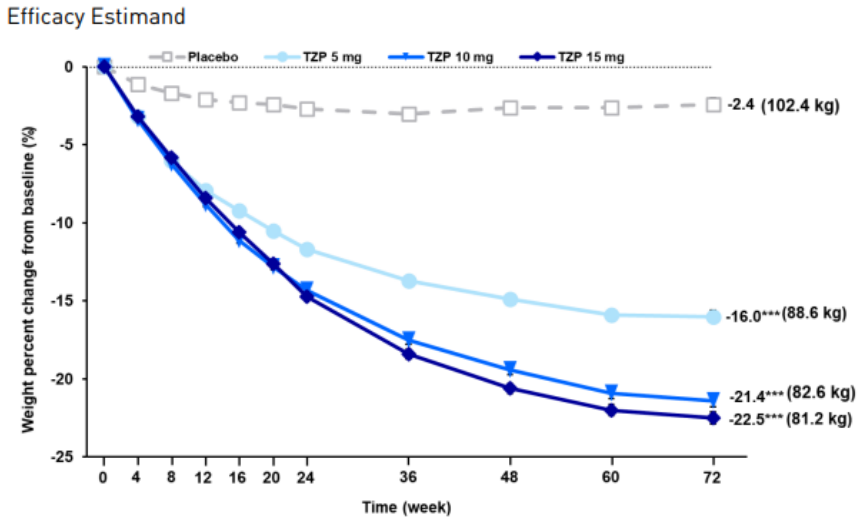
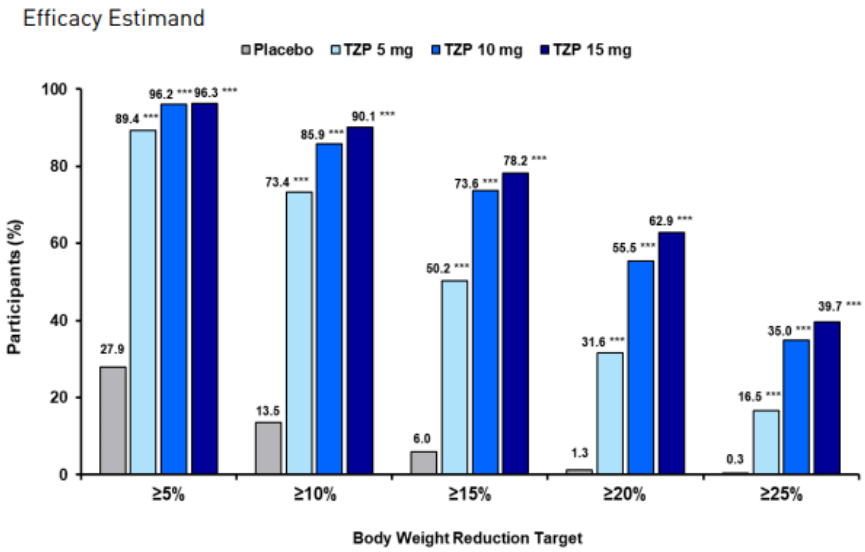
Incretins in diabetes and/or obesity

Eli Lilly – Tirzepatide – SURMOUNT-1 Phase 3 in obesity

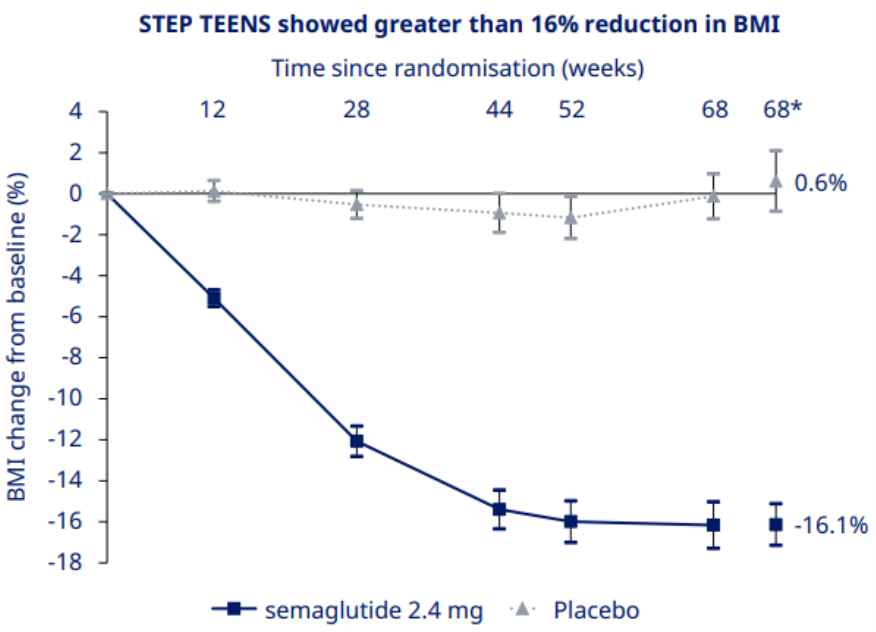
- SURMOUNT-1 Phase 3 trial testing 5, 10 & 15mg of tirzepatide in patients with obesity or overweight
  - GLP-1/GIP recently approved for T2D, under clinical development for other indications as obesity
  - Double blinded, placebo-controlled, 72 weeks, n=2,539
  - Inclusion: adults, BMI ≥ 30 kg/m² or ≥ 27 kg/m² with at least one comorbidities (hypertension, dyslipidemia, obstructive sleep apnea (OSA) or CV), no diabetes
  - Baselines: 44.9 years, Weight 104.8 ± 22.12 kg, BMI 38.0 ± 6.81 kg/m², 40.6% with prediabetes, eGFR 98.1 ml/min/1.73m²
  - Results:
    - Up to -22.5kg weight loss
    - Up to 96.3% of patients with ≥ 5% weight loss, 78.2% ≥ 15% & 39.7% ≥ 25%
    - Similar decrease of systolic blood pressure between doses (-7.0 to -8.2 mmHg vs -1.2mmHg)
    - Similar tolerability profile between doses with treatment discontinuation due to AE of 4.3% to 7.1% vs 2.6%
    - Overall treatment discontinuation of 14-16% vs 26% with placebo
- Slide of the corporate summary





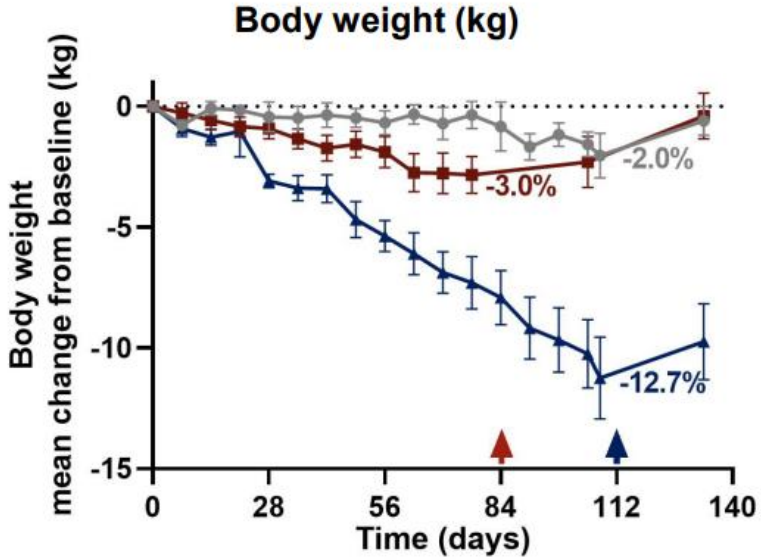
Novo Nordisk – Semaglutide – STEP TEENS Phase 3

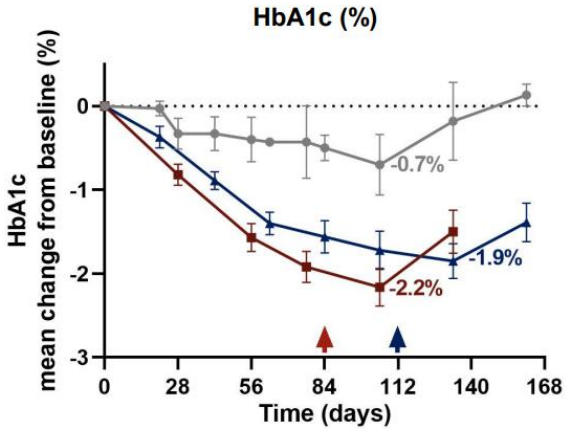
- STEP TEENS Phase 3 trial testing once weekly semaglutide 2.4 mg in patients with obesity or overweight
  - GLP-1 approved T2D and obesity in adults
  - Double blinded, placebo-controlled, 68 weeks, n=163
  - Inclusion: adolescent 12-17 years, BMI ≥ 95th percentile or ≥ 85th percentile with at least one comorbidities (hypertension, dyslipidemia, obstructive sleep apnea (OSA) or T2D), for T2D, A1c < 10%
  - Baselines: 15.4 years, BMI 37.0 kg/m²
  - Results:
    - **-16.1% vs +0.6% weight loss**
    - 72.5% of patients with ≥ 5% weight loss
    - Similar tolerability profile with adults Phase 3 trials
    - Improvement of IWQOL-Kids scores (+4.27, stat sign diff)
- Slide of the corporate summary



Eli Lilly – Mazdutide (GLP-1/Gluc) – Phase 1 in T2D

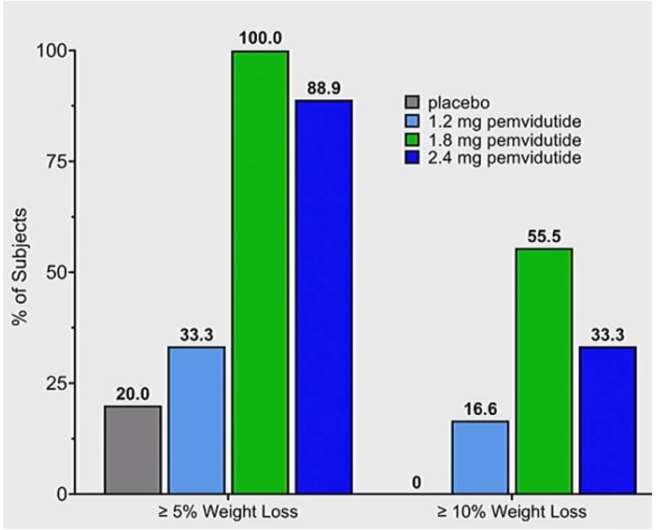
- Phase 1 trial testing Mazdutide (LY3305677) GLP-1 Glucagon agonist in T2D
  - GLP-1/Glucagon in Phase 1 development for T2D
  - Placebo-controlled, double-blinded, 16 weeks, n=24 T2D
  - Inclusion: 20-69 years, BMI 23-40 kg/m², weight < 150kg, no episodes of severe hypos in last 6 months
  - Baselines (range of the averages in the different arms): 55.7-61.4 years, A1c 7.7-8.5%, weight 94.7-97.5 kg
  - Results:
    - Safety, strong levels in the 10mg arm (cohort 2) of AE mainly GI
    - PK data supporting a once weekly dosing (8.8 days of half-life)
    - A1c: -2.2% (4.5mg) vs -1.9% (10mg) vs -0.7% (pl)
    - Weight: -3.0% (4.5mg) vs -12.7% (10mg) vs -2.0% (pl)
    - Improves insulin sensitivity reducing insulin demand
    - Reduces triglyceride & LDL cholesterol levels
- Another Phase 1 trial in healthy patients demonstrated similar safety and PK properties
- Slides

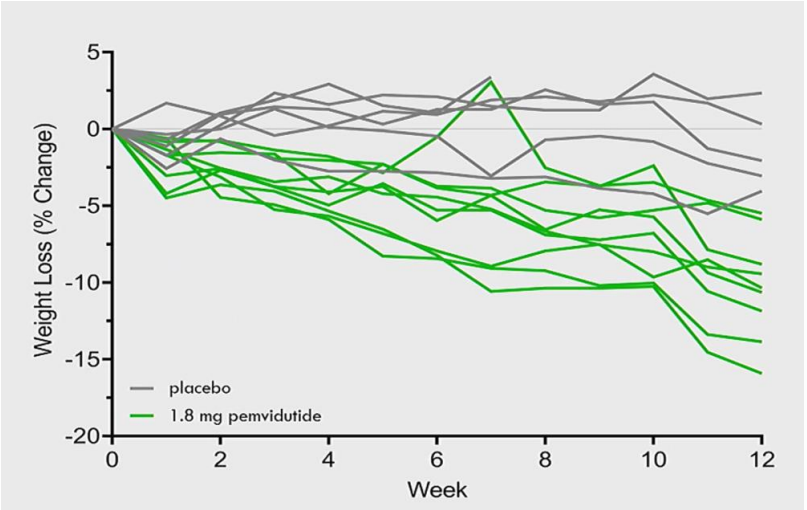




Altimmune – Pemvidutide (GLP-1/Gluc) – Phase 1 in Obesity

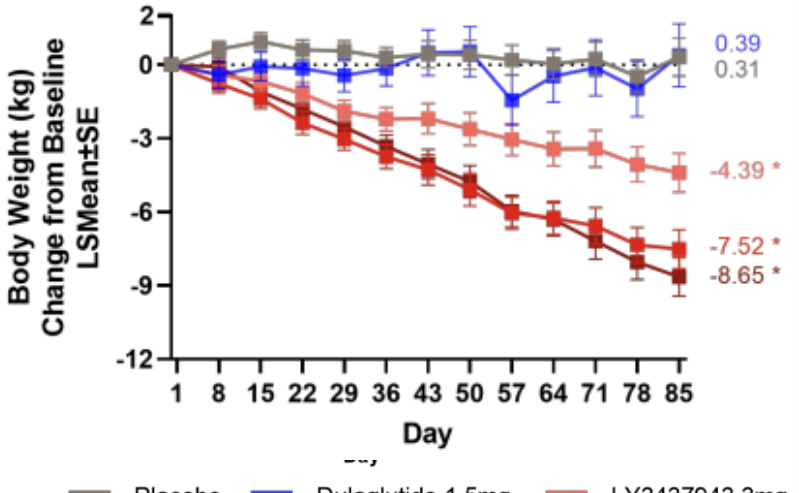
- Phase 1 trial (Part 2) testing Pemvidutide (ALT-801) GLP-1 Glucagon agonist in healthy overweight & obese
  - GLP-1/glucagon in Phase 2 for obesity & Phase 1 for NASH
  - Placebo-controlled, double-blinded, 12 weeks, n=34
  - 3 doses: 1.2, 1.8 & 2.4mg
  - Inclusion: 18-60 years, BMI 25-40 kg/m², MRI-PDFF ≥ 10%, no diabetes
  - Baselines (range of the averages in the different arms): 27.7-35.3 years, BMI 30.0-31.8 kg/m², A1c 5.3-5.5%,
  - Results:
    - Good safety, no withdrawals due to AE, GI effects similar to other GLP-1s
    - PK data supporting a once weekly dosing (110hrs of half-life)
    - Weight: -4.9% (1.2mg), -10.3% (1.8mg) & -9.0% (2.4Mg) vs -1.6% (pl)
    - 100% of patients with 1.8mg reach -5% of weight loss, 55.5% reach 10%
    - Reduces triglyceride & LDL cholesterol levels
    - Blood pressure improvement

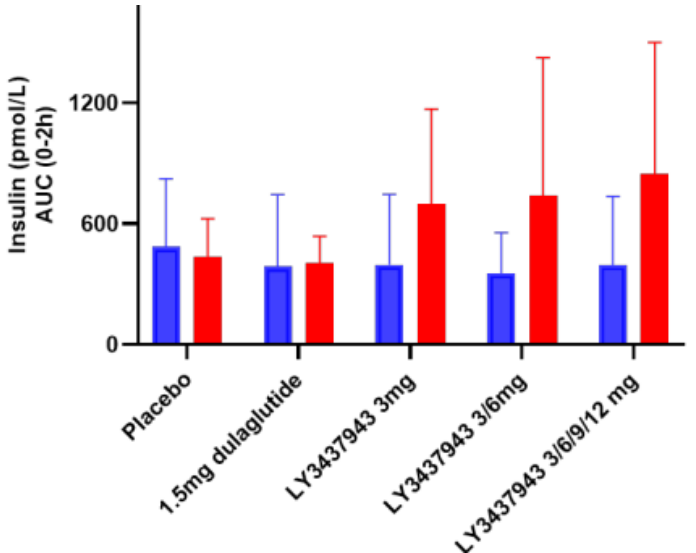




Ely Lilly – GIP/GLP-1/Glucagon – Phase 1 in T2D

- Phase 1 trial testing LY3437943 GGG triple agonist vs dulaglutide in T2D
  - Glucagon/GLP-1/GIP in Phase 2 for diabetes & obesity
  - Placebo-controlled, double-blinded, 12 weeks, n=72 T2D
  - Inclusion: 20-70 years, A1c 7-10.5%, BMI 23-50 kg/m², no episodes of severe hypos
  - Baselines (range of the averages in the different arms): 55.8-61.5 years, A1c 8.07-9.05%, weight 82.5-92.4 kg
  - Results:
    - Safety, strong levels in the 12mg arm of AE mainly GI, similar GI effects between the 6mg arm and the dulaglutide one
    - Significant decrease in systolic blood pressure (-7.99 mmHg with 6mg vs + 9.89mmHg with dulaglutide & -1.16 with placebo), similar trend with diastolic BP and increase of pulse rate
    - PK data supporting a once weekly dosing (6 days of half-life)
    - -1.9%* A1c (6mg) vs -0.96% (dula) vs -0.34% (pl)
    - -7.52 kg* (6mg) vs +0.39 kg (dula) vs +0.31 kg (pl)
    - Improves insulin secretion
  - Slides





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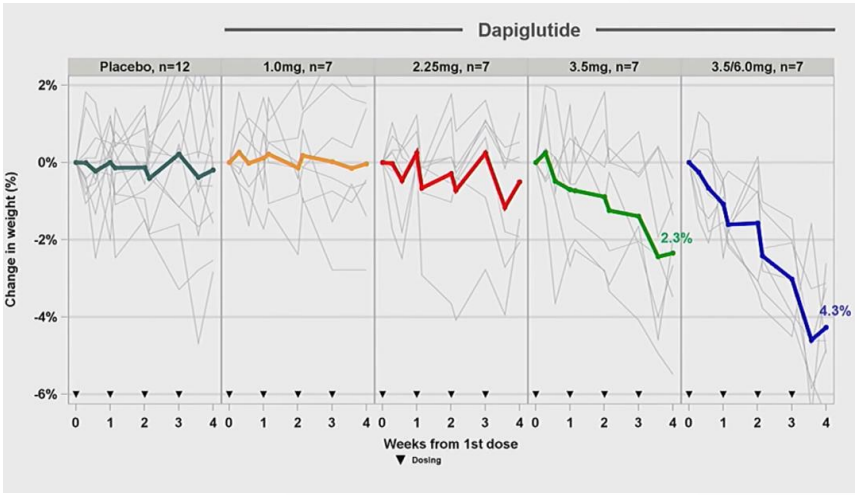
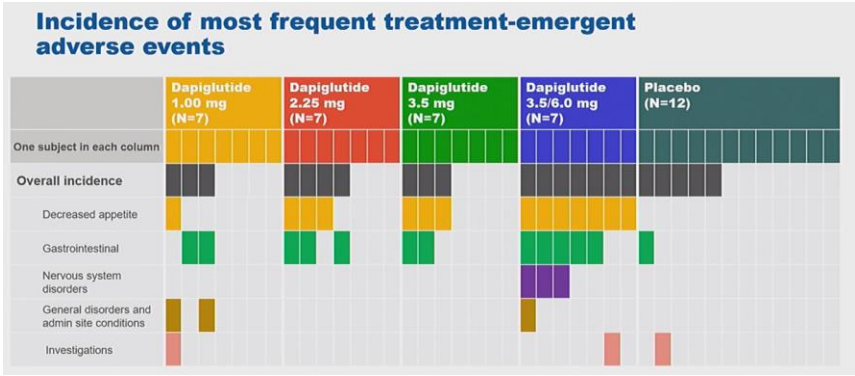
* p<0.05 vs placebo

Zealand – Dapiglutide (GLP-1/GLP-2) – Phase 1 in Healthy

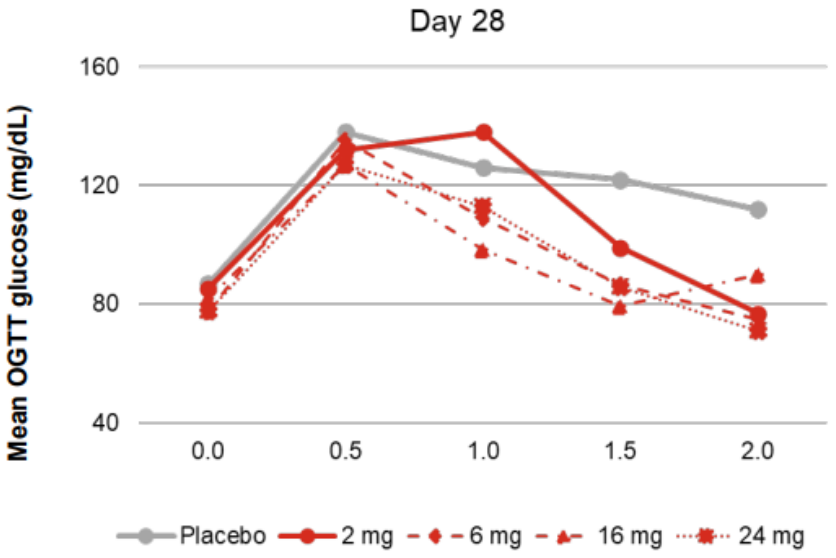
- Phase 1 trial testing Dapiglutide (ZP7570) GLP-1 GLP-2 agonist in healthy
  - GLP-1/GLP-2 co-agonist in Phase 1 for obesity
  - Placebo-controlled, double-blinded, 4 weeks, n=40
  - 4 doses: 1.0, 2.25, 3.5 & 6.0mg
  - Inclusion: 18-55 years, healthy, BMI 18.5-28 kg/m², no diabetes
  - Baselines: 34 years, BMI 24.6 kg/m², weight 78.3 kg
  - Results:
    - Good safety, no withdrawals due to AE, GI effects similar to other GLP-1s
    - PK data supporting a once weekly dosing (123-129hrs of half-life)
    - Weight: -2.3% (3.5mg), -4.3% (6.0mg) vs no significant change with placebo
    - Strong reduction of food intake with the 6.0mg dose (~-40% after the 4th dose)
    - Gastric emptying reduction (dose dependent)
    - Insulin and glucose reduction





Eli Lilly – Oral GLP-1 NPA – Phase 1

- Phase 1 trial testing once daily Oral GLP-1 (LY3502970) in T2D
  - Oral GLP-1 in Phase 2 for diabetes & obesity
  - Placebo-controlled, double-blinded, 12 weeks, n=69 T2D
  - Inclusion: 18-70 years, A1c 7.0-10.5%, BMI 18.5-45 kg/m², weight ≥ 45kg
  - Baselines: 43.4-42.5 years, weight 84.5-83.5 kg
  - Results:
    - Safety, coherent GI AE effects, no serious AE
    - PK approximately dose proportional
    - Improved OGGT (oral glucose tolerance test) compare to placebo in part B
    - Weight: up to -3.6kg vs placebo with higher dose (24mg), sign diff
- Slides



	AUC(0-2h) LSM at Day 28	Difference in LSM vs. placebo (90% CI)
Placebo (n=14)	240.2	-
2 mg (n=8)	198.3	-41.9 (-65.6, -18.3)
6 mg (n=9)	200.0	-40.2 (-62.8, -17.6)
16 mg (n=8)	210.9	-29.4 (-52.9, -5.8)
24 mg (n=8)	223.5	-16.8 (-40.5, 7.0)
24 mg (n=8)	196.4	-43.8 (-67.3, -20.4)

Semagultide in obese/overweight T1D

- Independent trial testing semaglutide 1mg in n=20 adults overweight/obese T1D, during 6 months
- Baselines: 46.3 years, BMI 33 kg/m², A1c 7.4%
- Results:
  - -8.5kg weight loss
  - 60% with weight loss > 5%
  - 40% with weight loss > 10%
  - 0.3% A1c reduction

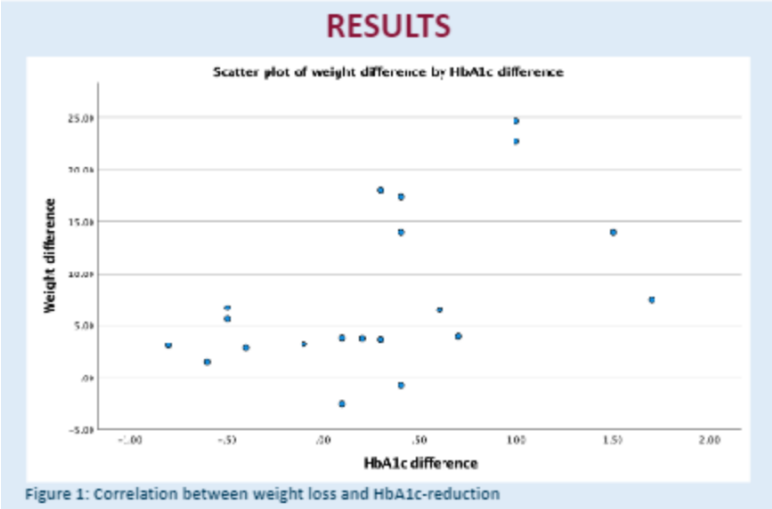
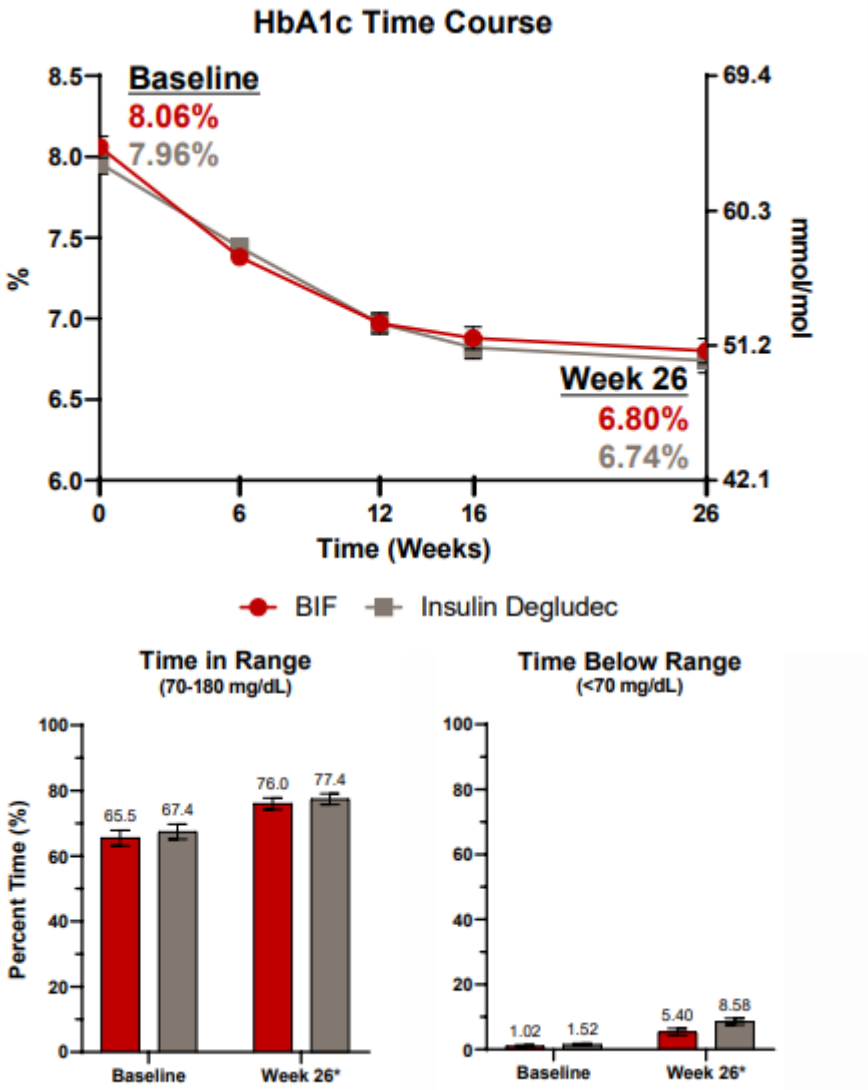


Figure 1: Correlation between weight loss and HbA1c-reduction

Weekly basal insulins

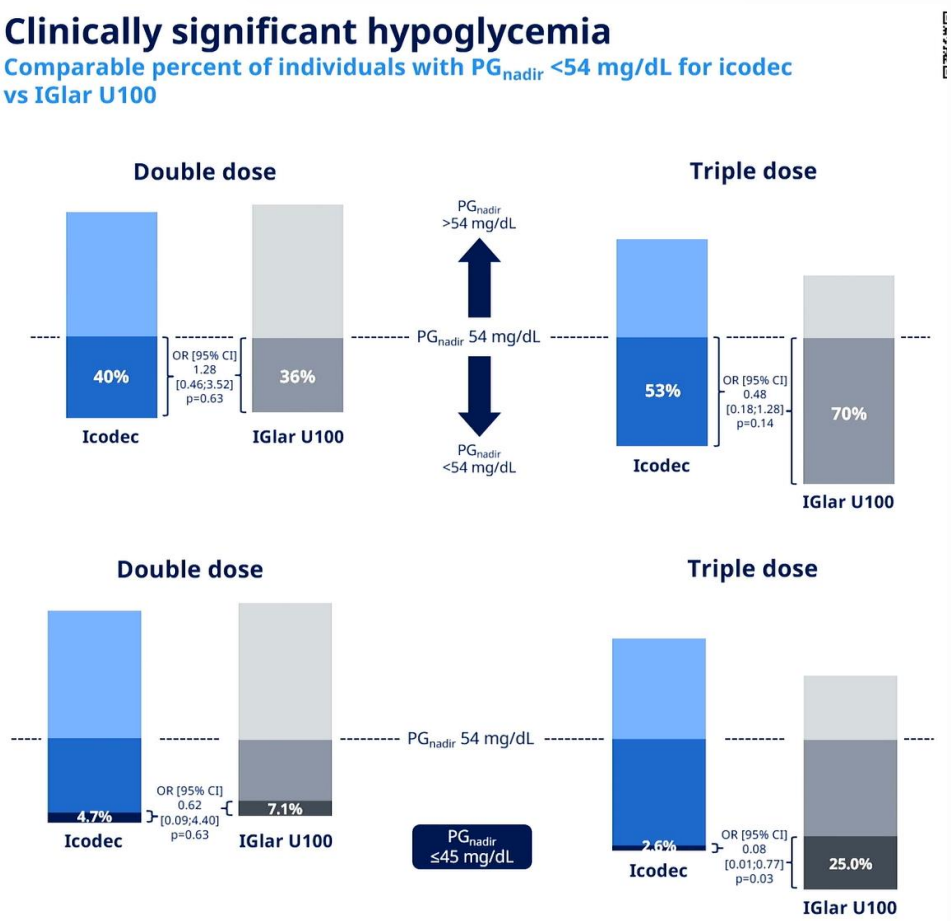
Eli Lilly – Basal Insulin FC – Phase 2 in T2D

- Phase 2 trial testing BIF insulin vs degludec in insulin naïve T2D
  - Weekly basal insulin in Phase 3 for T2D
  - Open-label, 26 weeks, n=278
  - Inclusion: 18-75 years, using metformin w/o DPP4 and/or SGLT2 for 3 months, A1c 7-9.5%, BMI 20-45 kg/m²
  - Baselines: 59.4-57.3 years, 8.0-8.1% A1c, 90.6-91.0 kg weight, 54.8-60.8% using metformin only
  - Results:
    - -1.2% vs -1.26% A1c (non sign.) reaching 6.80% vs 6.74%
    - 62.3% vs 68.6% with A1c < 7%
    - 76.0% vs 77.4% TIR (from 65.5% & 67.4%)
    - Similar safety profiles
    - Slight increase of level 1 hypo occurrences (3.29 vs 2.77 rate/patient/year, stat. sign. not provided)
- Slides of the presentation



Novo Nordisk – Icodec insulin – Phase 1 with insulin overdose

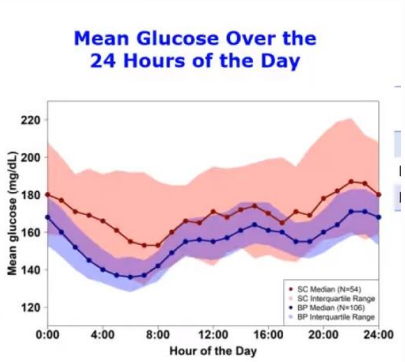
- Phase 1 trial testing overdoses of once weekly insulin Icodec vs glargine in T2D
  - Weekly basal insulin in Phase 3 for diabetes
  - Cross-over, open-label, 6 weeks + 11 days, n=43
  - Inclusion: 18-72 years, BMI 18.5-37.9 kg/m², A1c ≤ 9%, total daily insulin 0.2-1.0 UI/kg/day
  - Baselines: 56.3 years, A1c 7.2%, Weight 87.1 kg, once daily glargine doses 0.35 UI/kg
  - Results:
    - Similar proportion of patients with hypoglycemia reduction when insulin doses doubled, slightly higher hypoglycemia with glargine when doses are tripled
    - Similar mean nadir plasma glucose
    - Greater adrenaline & cortisol responses and a trend towards greater noradrenaline response for icodec
- Slide of the corporate summary
- Novo Nordisk released in parallel of the conference the results of 3 ONWARDS Phase 3 trials (1, 2 & 6) showing similar A1c reduction than the comparator (cf corporate slides)

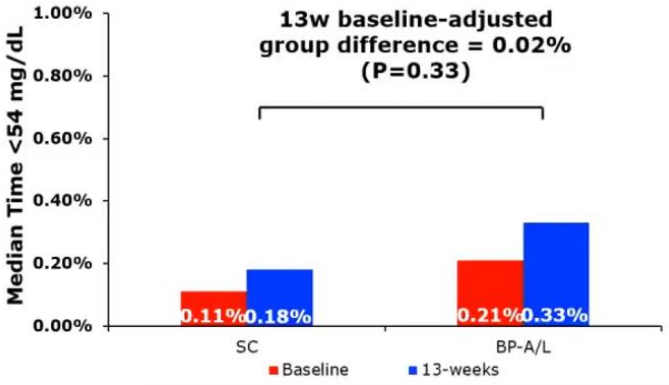


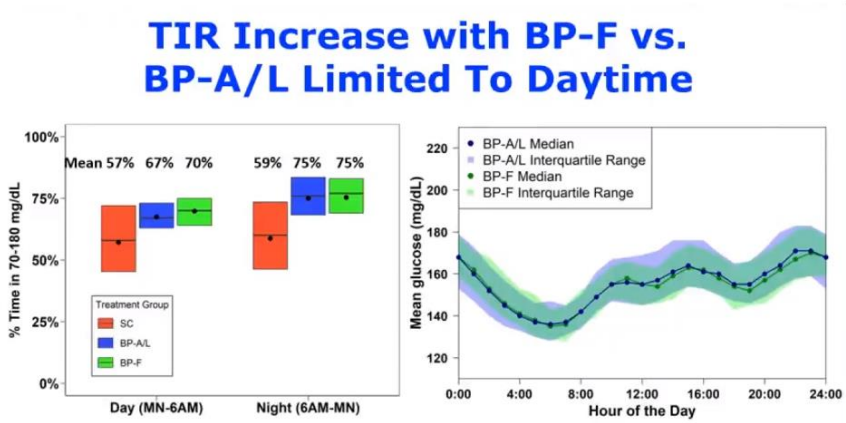
Devices – AID, CGMs & smart pens

Beta Bionics – insulin-only iLet – pivotal - Adults

- Pivotal trial testing the insulin-only iLet system with aspart or lispro vs standard of care
  - Open-label, 13 weeks, n=161 adults
  - Inclusion: 18+ years, > 1 year with T1D, no A1c restrictions
  - Baselines: 44 years, 83% using CGM, 36% an hybrid closed-loop system, A1c 7.6%
  - Results:
    - 96% time in auto-mode, 90% auto-mode with CGM input
    - A1c improvement 7.1% vs 7.5% p<0.001
    - Non significant increase of time < 54 mg/dl
    - +11% increase TIR: 69% vs 58%
    - No total daily insulin changes
    - Non sign. higher number of severe hypoglycemia: 25.5 events/100 pers years vs 14.2
  - In another arm using Fiasp instead of Lispro or Aspart, results are similar with small improvement of TIR during the day (about 3%)

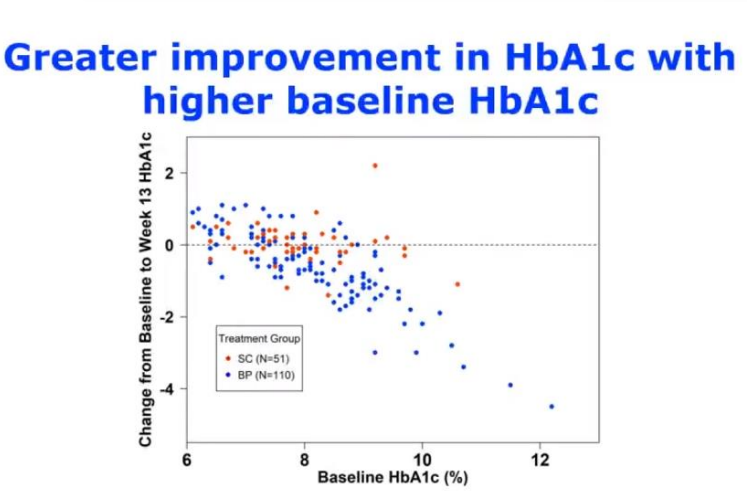


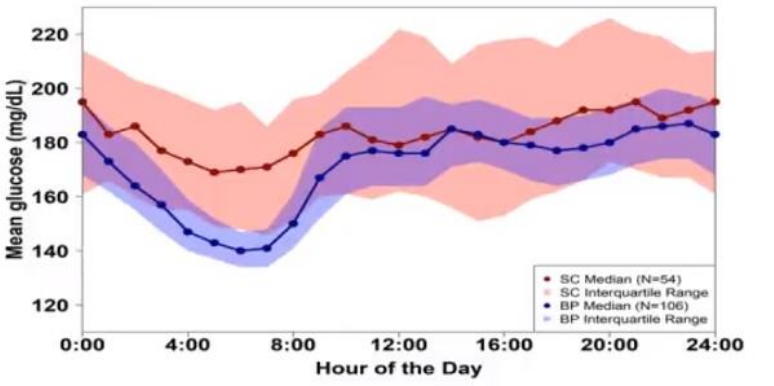




Beta Bionics – insulin-only iLet – pivotal - Pediatric

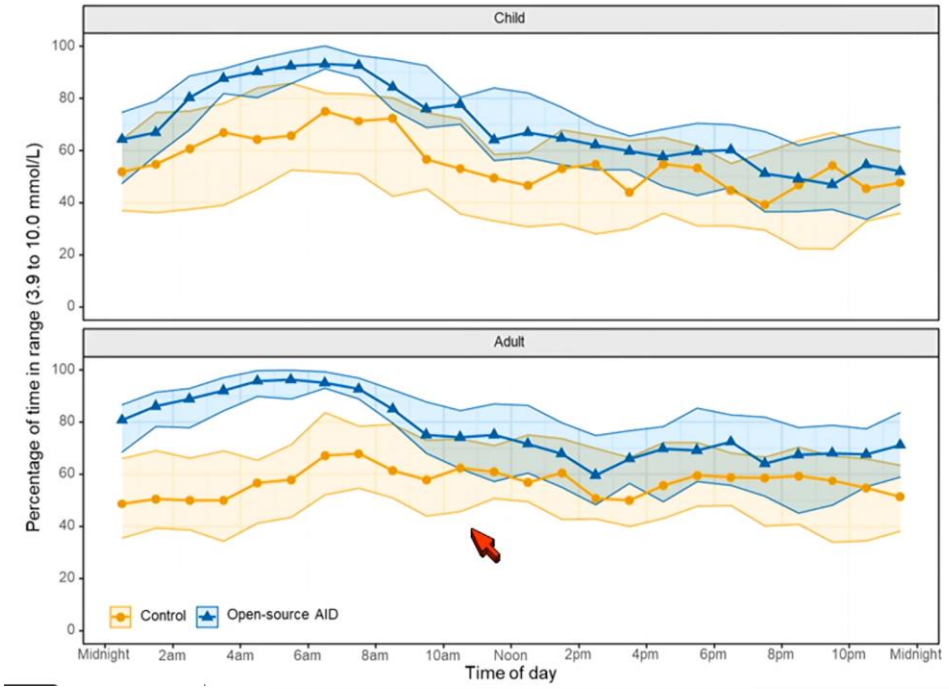
- Pivotal trial testing the insulin-only iLet system with aspart or lispro vs standard of care
  - Open-label, 13 weeks, n=165 pediatrics
  - Inclusion: 6-17 years, > 1 year with T1D, no A1c restrictions
  - Baselines: 12 years, 95% using CGM, 25% an hybrid closed-loop system, A1c 8.0%
  - Results:
    - 96% time in auto-mode, 89% auto-mode with CGM input
    - A1c improvement 7.5% vs 7.8% p<0.001
    - Non significant difference of time < 54 mg/dl
    - +10% increase TIR: 60% vs 50%
    - Slight increase of total daily insulin in both arms
    - Similar number of severe hypoglycemia: 10.4 events/100 pers years vs 7.3





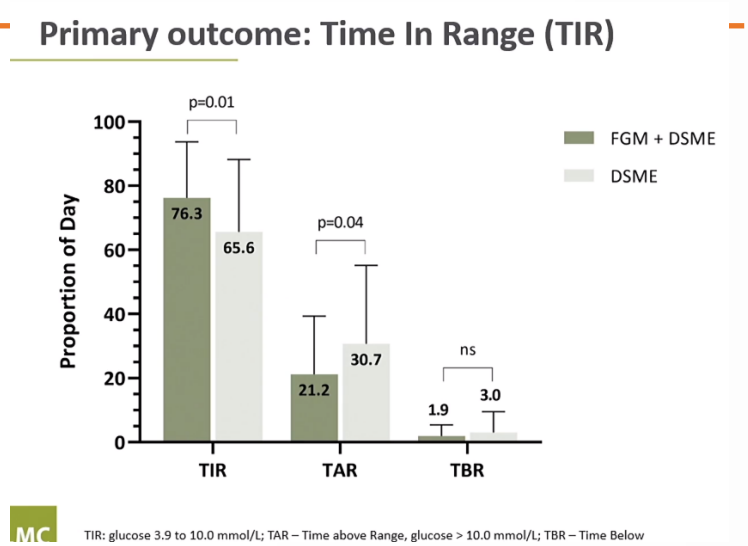
Do-it-Yourself – CREATE RCT

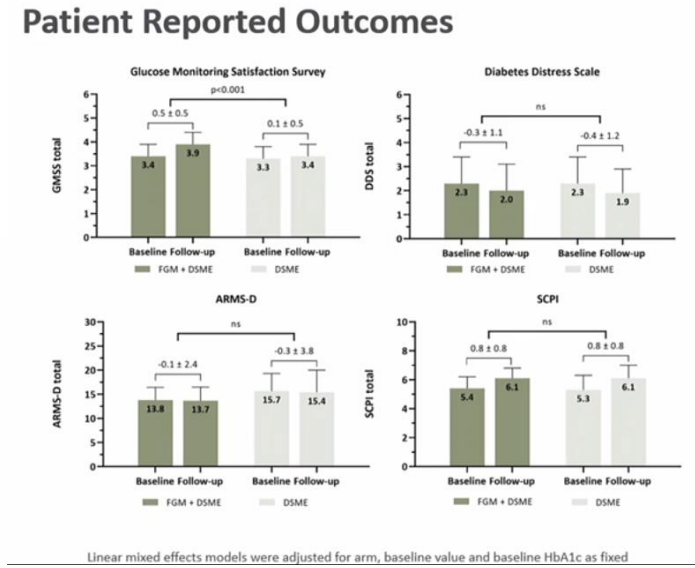
- Randomized trial testing AnyDANA-loop vs SAP (sensor augmented insulin pump) in T1Ds
  - The AnyDANA-loop consists of a smartphone app operating an open-source algorithm, an insulin pump, and a CGM
  - Open-labelled, 6 months, n=97
  - Inclusion: 7-70 years, insulin pump for > 6 months, A1c < 10.5%
  - Baselines Children (< 16 years): 13.0 years, A1c 7.5%, 56.1% TIR
  - Baselines Adults (≥ 16 years): 40.0 years, A1c 7.7%, 62.4% TIR
  - Results:
    - 14% TIR improvement, p<0.001
      - 71.2% from 61.2% in the AID arm, 54.4% from 57.7% in the control arm
    - 60% patients with A1c > 70% vs 15%
    - No severe hypo or DKA
    - Similar adverse events
    - AID system active 94% of the time



Abbott – Libre Freestyle - IMMEDIATE trial in non-insulin T2D

- Trial testing Libre Freestyle in non-insulin T2D with diabetes self management education vs BGM + DSME (diabetes self-management education)
  - Crossover, 2 parts, 16 weeks, n=116 T2D
  - Inclusion: 18+ years, A1c > 7.5%, no CGM, no use of insulin during past 3 months
  - Baselines: 59.2 & 57.6 years, A1c 8.4 & 8.6%, use of GLP-1 (28 & 35%), SGLT-2 (35 & 43%), DPP-4 (43 & 47%), SU (55 & 43%) & metformin (100 & 97%)
  - Results:
    - Improved TIR →
    - Improved A1C: 7.6% vs 8.1%, p=0.048
    - No main differences in therapies changes
    - Greater device satisfaction, no deterioration of diabetes distress





Bigfoot – Unity – Real-World data

- Retrospective analysis, BURST, of n=49 T1D or T2D users of Bigfoot Unity during 90 days after initiation
- Bigfoot Unity is a smart pen coupled with a phone app with doses recommendations
- Inclusion: 12+ years, MDI
- Baselines: 60.3 years, 82% T2D, 79.2UI/day, 72% used CGM in the past, A1c 8.5%
- Results:
  - GMI reduction to 7.5% at 90 days, from a A1c baseline of 8.5%
  - 59.1% of TIR at day 60 with 1.5% TBR (no baseline
  - Slight decrease of TIR, GMI and number of boluses during last month compared to the 1st 2 weeks on the devices with significative reduction of patient engagement (14.7 interactions/patient/day last months vs 21.7 during 1st 2 weeks)

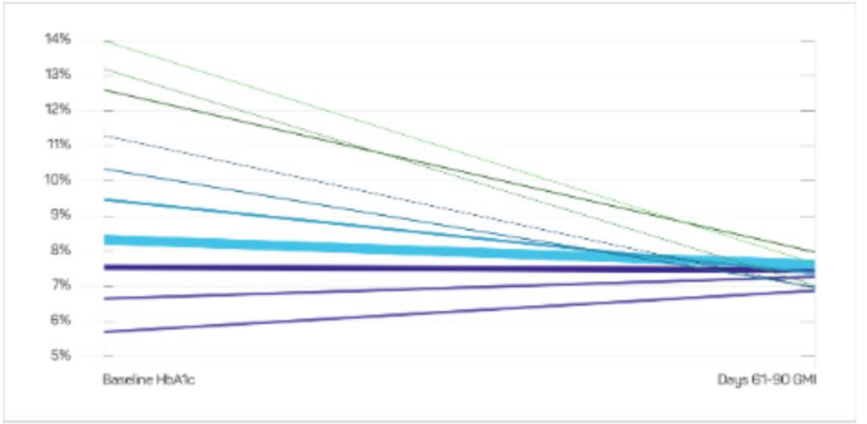


Figure 1 Change plot for baseline HbA1c to GMI in the 3rd month for various starting HbA1c levels within the overall cohort (N=43). Thickness of line represents the number of individuals in each HbA1c level.

Analysis provided by Sam Collaudin

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- Don’t hesitate to contact me for feedbacks, comments, or questions