Kinexum EASD 2022 report

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Sept 19-22, 2022

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- It synthesizes selected data presented during the EASD 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).
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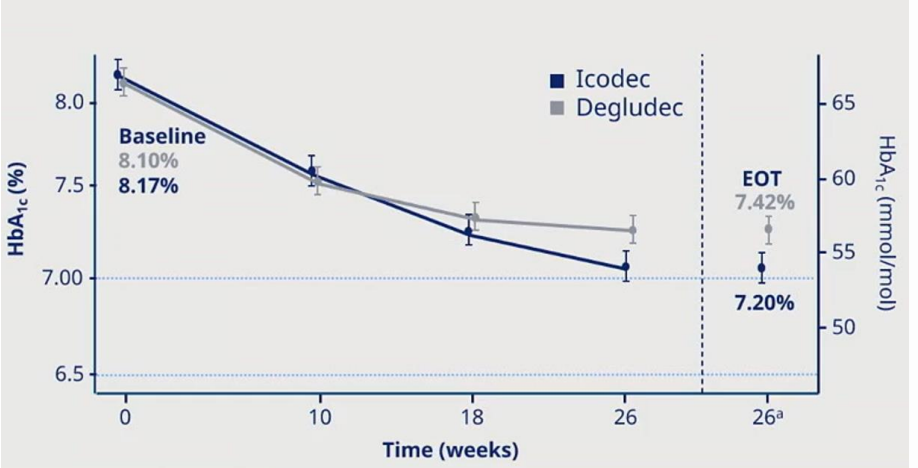
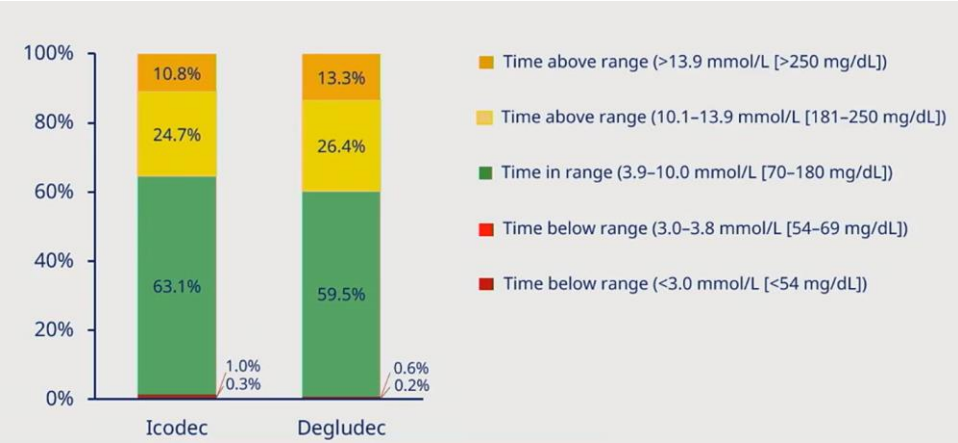
Table of content

Insulins

Novo Nordisk – Icodec - Onwards 2

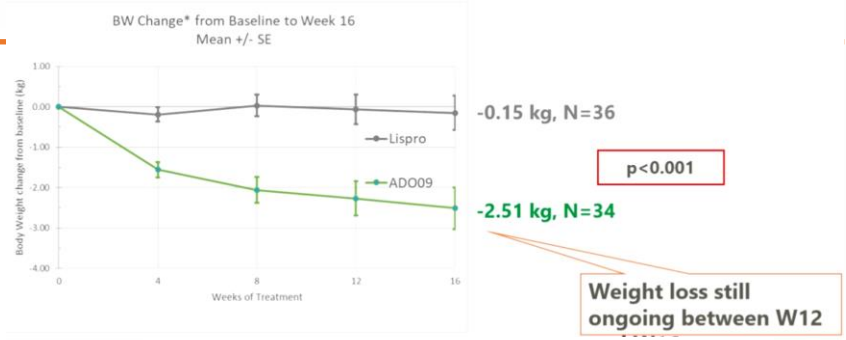
- Novo presented first **detailed results** of a Phase 3 **Onwards 2** with the **weekly basal insulin Icodec**
- Open-label trial testing **insulin Icodec** vs **insulin Degludec** in **n=526 T2D** during **26 weeks**
- **Inclusion criteria**: ≥ 18 years, A1c 7-10%, Using basal insulin (no prandial) w/o OADs, BMI ≤ 40 kg/m²
- **Baselines**: **A1c 8.17%** (Icodec) vs **8.10%**
- **Results**:
  - **A1c change**: -0.93% (Icodec) vs -0.71%, p=0.0028
  - **TIR**: 63.1% vs 59.5% (no statistically significant difference)
  - **TBR**: 1.3% vs 0.8% (no statistically significant difference)
  - **Level 2 hypos**: 0.73 events/person/year vs 0.27, Estimated rate ratio of 1.98, p = 0.0677
  - **A1c < 7% without level 2 or 3 hypos**: 36.7% vs 26.8% p=0.0223
  - **DTSQ**: 4.22 vs 2.96, p=0.0036

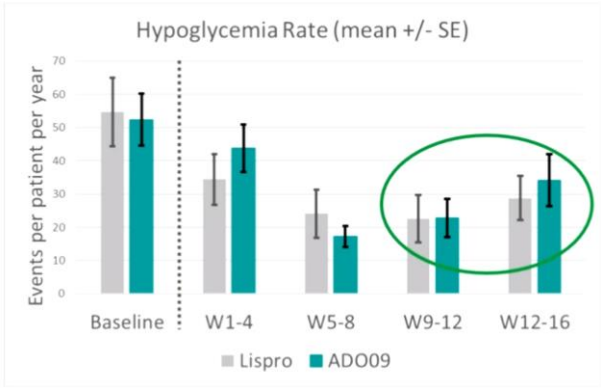


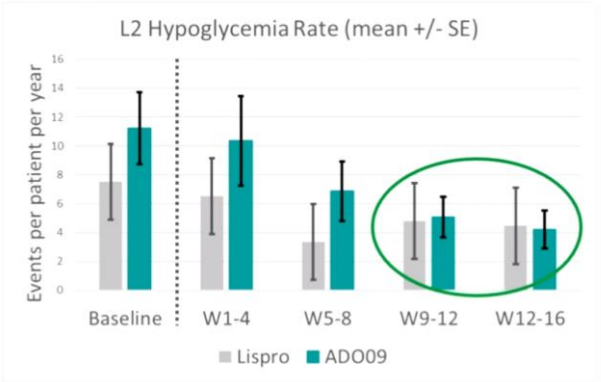


Adocia – ADO09 – pramlintide/insulin – Phase 2

- Results of a Phase 2, open-labelled, trial testing **ADO09** (combination of **human prandial insulin with pramlintide** at a ratio of 6µg/UI) vs insulin lispro in **n=80 T1D** during **16 weeks**
- **Inclusion criteria**: 18-64 years, T1D ≥ 12 months, A1c 7-9.5%, BMI 25-35 kg/m², MDI
- **Baselines**: 43.1 (ADO09) & 45.2 years, **A1c 7.7%,** weight 88.7 & 91.8 kg, 28.8 vs 29.7 units of prandial insulin / day
- **Results**:
  - **-2.51 kg (ADO09) vs -0.15kg, p<0.001**
  - No differences of hypoglycemia after week 9
  - 40% vs 7.5% with GI side effects -> 2 patients discontinuated ADO09
  - **A1c change** : +0.14% vs +0.10%, p=0.81
  - **TIR**: -3.17% vs -1.54%, p=0.29
  - **Prandial insulin dose**: -5.97UI/day vs -0.61UI/day, p<0.001
  - Satiety effect through a questionnaire: 82.4% vs 43.2%, p<0.001

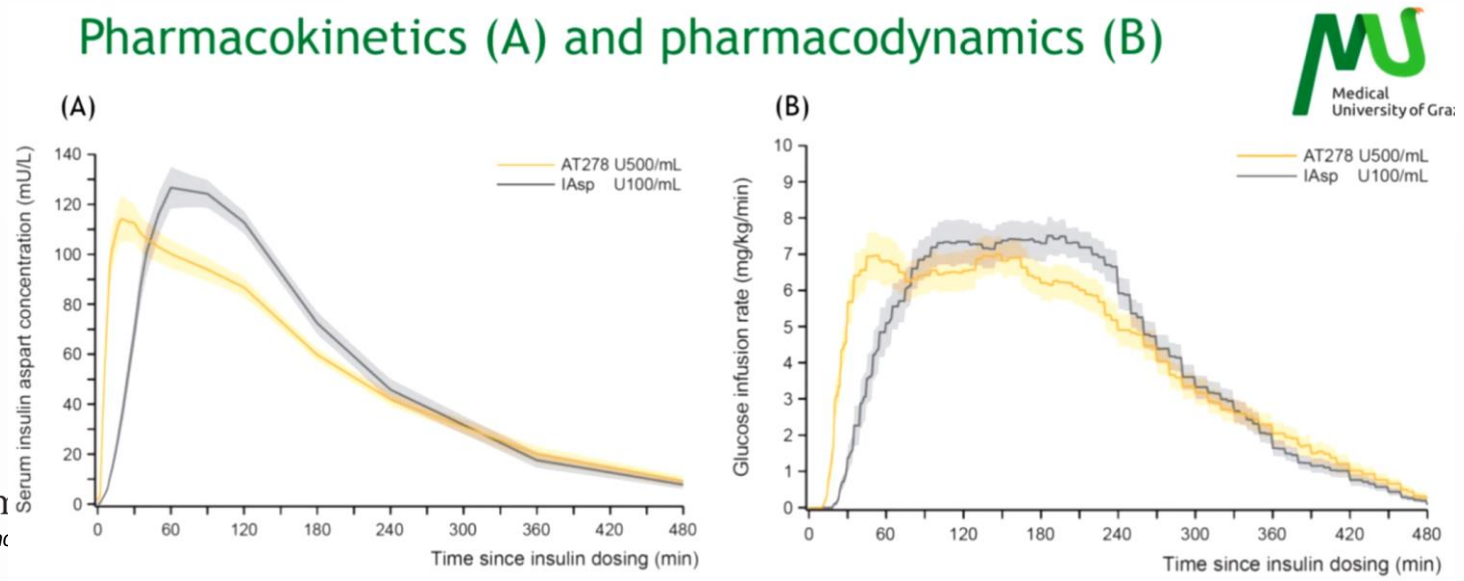






Arecor – AT278 – URI aspart U500 – Phase 1

- Results of a Phase 1, double-blinded, single-dose, randomized, two-way crossover, glucose clamp study trial testing **AT278** (an **ultra rapid U500 aspart prandial insulin**) vs **aspart insulin** in **n=38 T1D**
- **Inclusion criteria**: 18-64 years, using insulin for ≥ 12 months, A1c ≤ 8.5%, weight 75-100kg
- **Baselines**: 38.8 years, **A1c 7.0%,** Weight 86.4 kg



Incretins

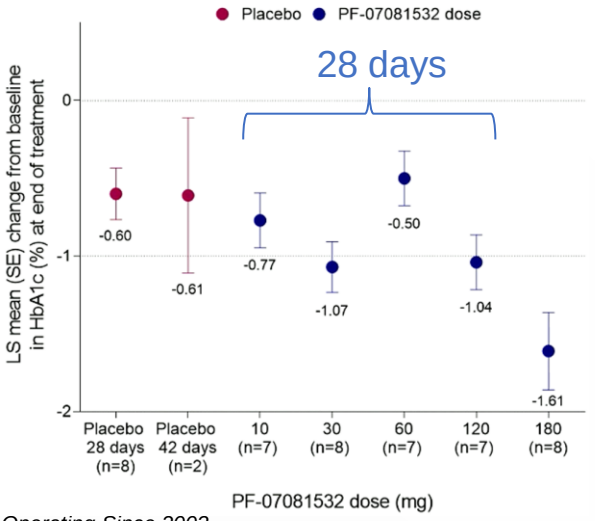
Pfizer – Danuglipron – Oral GLP-1 – Phase 2

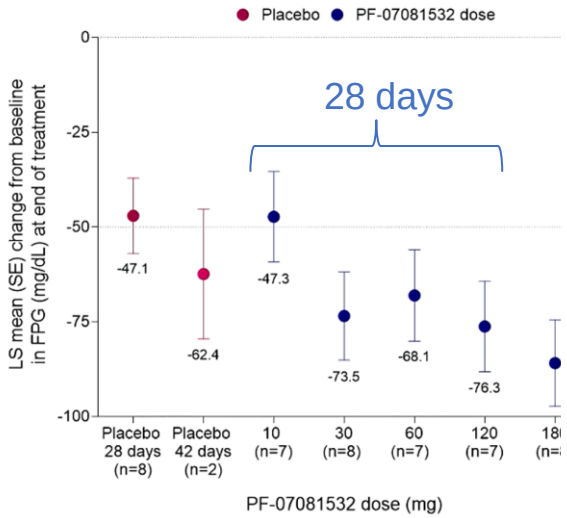
- Results of 2 trials testing **danuglipron**, an **oral GLP-1**

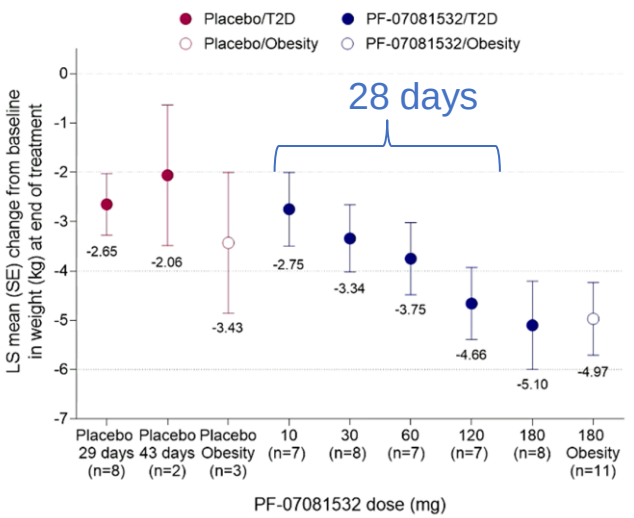
Trial	NCT046172775 – Phase 2a		NCT03985293 – Phase 2b
Type	Double-blind, placebo-controlled		Double-blind, placebo-controlled
Duration	12 weeks		16 weeks
Patients	N=123 **T2D**	N=28 **obese without T2D**	N=411 **T2D**
Doses	80 to 200mg BID	200mg BID	2.5 to 200 mg BID
Inclusion criteria	18-75 years, T2D with metformin, A1c 7 – 10.5%, BMI ≥ 27 kg/m²	18-75 years, A1c < 6.5%, FPG < 126 mg/dL, BMI ≥ 30 kg/m²	18-75 years, T2D w/o metformin, A1c 7-10.5%, BMI 24.5-45.4 kg/m²
Baselines	58.3 years, **A1c = 8.19%**, FPG = 171.82 mg/dL, Weight = 95.5 kg, BMI = 33.9 kg/m²	48.7 years, **weight = 102.9 kg**, BMI = 37.3 kg/m²	58.6 years, 91.5% using metformin, **A1c = 8.07%,** FPG = 169.3 mg/dL, weight = 91.3 kg, BMI = 32.8 kg/m²
Discontinuations due to AE	**18.2% to 38.1% vs 6.3**%	**54.5% vs 0%**	**2.9% to 33.8% vs 7.6%**
A1c reduction	Between **-1.04 & -1.57% vs -0.32%, all p<0.05 vs pl**		**-0.49% to -1.18% vs -0.02%, all p<0.1**
FPG	-23.34 to -53.94 mg/dL vs -13.09 mg/dL, all except 120mg BID HF p<0.05 vs pl		-12.81 to -31.93 mg/dL vs + 1.31 mg/dL, all p<0.1
Weight	**-1.93 to -5.38 kg vs -0.42 kg, all except 80mg BID HF p<0.05**	**-7.17 kg vs -0.30 kg, p=0.0826**	**+0.02kg to -4.60kg vs -0.43kg, 80 & 200mg BID with p<0.1**

Pfizer – PF-07081532 – oral GLP-1 – Phase 1

- Results of a Phase 1, double-blinded, placebo-controlled, trial testing daily 10 to 180 mg of a **new oral GLP-1** (different from Danuglipron) in **n=16 T2D** (8 during **28 days** & 8 during **42 days**) & **n=12 obese (42 days)**
- **Inclusion criteria:**
  - T2D: metformin, A1c 7-10.5%, BMI 24.5-45.5 kg/m²
  - Obese: A1c < 6.5% & BMI 30.5-45.5kg/m²
- **Baselines:**
  - T2D: 58.6 years, **A1c 8.6%**, weight 89.7 kg, BMI 32.1 kg/m², FPG 194.1 mg/dL
  - Obese: 53.3 years, A1c 5.6%, **weight 98.2kg**, BMI 32.9 kg/m²
- **Results:**
  - AE coherent with oral GLP-1s
  - Half-life supporting once daily administration (20.7-26.5 hours)



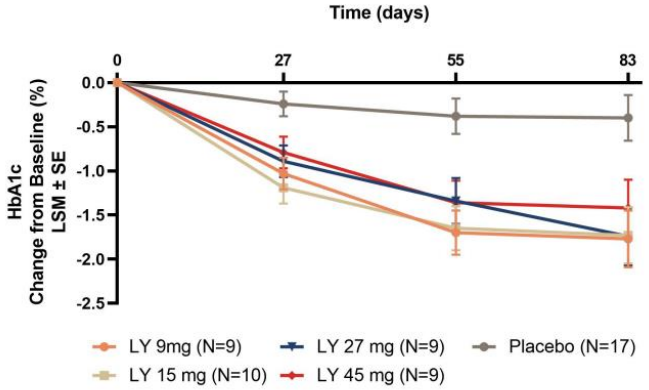


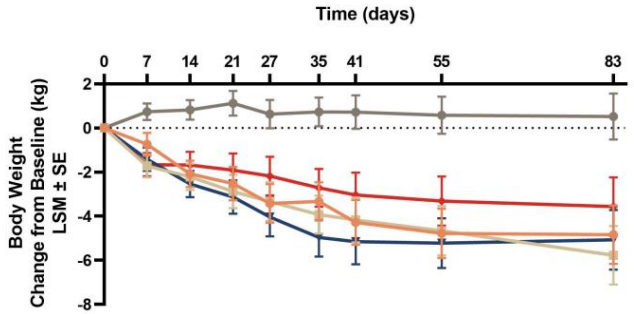


Eli Lilly – LY3502970 – Oral GLP-1 – Phase 1

- Double-blind, placebo-controlled Phase 1 trial with 5 cohorts
- **N=68 T2**D using 9 to 45 mg daily of **oral GLP-1** during **12 weeks**
- **Inclusion criteria**: 18-70 years, A1c 7-10.5%, BMI 18.5-45 kg/m²
- **Baselines** (LY & pl): 58.5 & 65 years, **A1c = 8.0 & 8.1%,** weight = 88.4 & 90.3kg, BMI = 30.9 & 31.3 kg/m², FPG = 172.6 & 162.9 mg/dL
- Results:

Treatment	LY 9mg	LY 15mg	LY 27mg	LY 45mg	Placebo
A1c change	**-1.77%**	**-1.73%**	**-1.74%**	**-1.42%**	**-0.40%**
FPG (mg/dL)	-3.00	-2.85	-2.42	-2.29	-1.14
Weight (kg)	**-4.84**	**-5.77**	**-5.07**	**-3.56**	**+0.52**
Nausea	44.4%	50.0%	33.3%	77.8%	5.9%

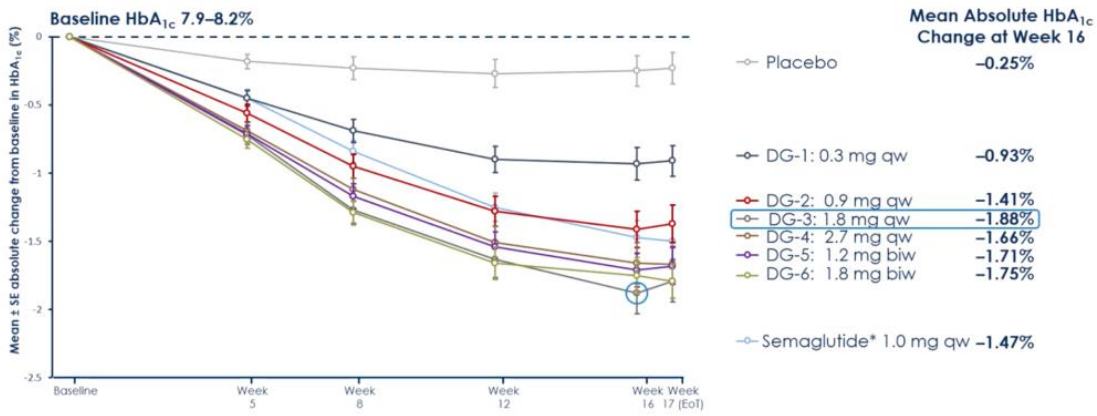




Incretins

BI/Zealand – BI-456906 – GLP-1/Glucagon – Phase 2

- Results of a Phase 2, double-blinded, randomized, parallel group, dose-finding, placebo-controlled, trial testing different doses/ regimens of BI/Zealand **GLP-1/glucagon co-agonist** vs **semaglutide** in **n=411 T2Ds** during **16 weeks**
- **Inclusion criteria**: 18-75 years, T2D ≥ 6 months, A1c 7-10%, BMI 25-50 kg/m², on metformin
- **Baselines**: **A1c 7.9-8.2%**
- Robust weight reduction presented at the Obesity week



Adverse events n (%)	DG-1 0.3 mg qw (n=50)	DG-2 0.9 mg qw (n=50)	DG-3 1.8 mg qw (n=52)	DG-4 2.7 mg qw (n=50)	DG-5 1.2 mg biw (n=51)	DG-6 1.8 mg biw (n=49)	Semaglutide 1.0 mg qw* (n=50)	Placebo (n=59)	Total BI 456906 (n=302)
Any TEAE	33 (66.0)	38 (76.0)	42 (80.8)	41 (82.0)	39 (76.5)	42 (85.7)	26 (52.0)	31 (52.5)	235 (77.8)
Investigator-defined drug-related AEs	25 (50.0)	26 (52.0)	33 (63.5)	29 (58.0)	28 (54.9)	36 (73.5)	19 (38.0)	13 (22.0)	177 (58.6)
Nausea	10 (20.0)	13 (26.0)	24 (46.2)	20 (40.0)	14 (27.5)	22 (44.9)	6 (12.0)	5 (8.5)	103 (34.1)
Vomiting	6 (12.0)	7 (14.0)	12 (23.1)	13 (26.0)	6 (11.8)	10 (20.4)	2 (4.0)	1 (1.7)	54 (17.9)
Diarrhoea	11 (22.0)	5 (10.0)	8 (15.4)	7 (14.0)	8 (15.7)	9 (18.4)	4 (8.0)	5 (8.5)	48 (15.9)
Dyspepsia	4 (8.0)	3 (6.0)	3 (5.8)	4 (8.0)	3 (5.9)	6 (12.2)	1 (2.0)	0	23 (7.6)
Decreased appetite	6 (12.0)	7 (14.0)	5 (9.6)	9 (18.0)	8 (15.7)	15 (30.6)	3 (6.0)	2 (3.4)	50 (16.6)
Injection site reaction‡	1 (2.0)	1 (2.0)	1 (1.9)	3 (6.0)	2 (3.9)	4 (8.2)	2 (4.0)	1 (1.7)	12 (4.0)
Serious AEs	1 (2.0)	4 (8.0)	3 (5.8)	2 (4.0)	1 (2.0)	0	0	3 (5.1)	11 (3.6)
Drug-related serious AEs‡	1 (2.0)	1 (2.0)	1 (1.9)	1 (2.0)	0	0	0	0	4 (1.3)
AEs leading to treatment discontinuation	5 (10.0)	5 (10.0)	11 (21.2)	15 (30.0)	4 (7.8)	8 (16.3)	2 (4.0)	3 (5.1)	48 (15.9)

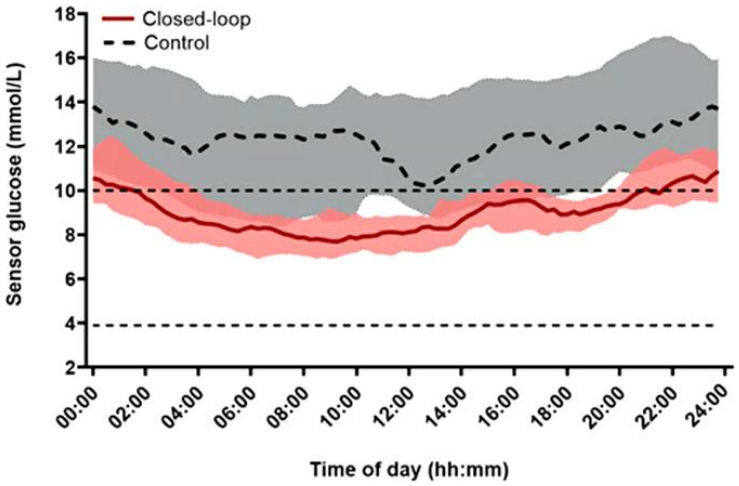
Others in drugs

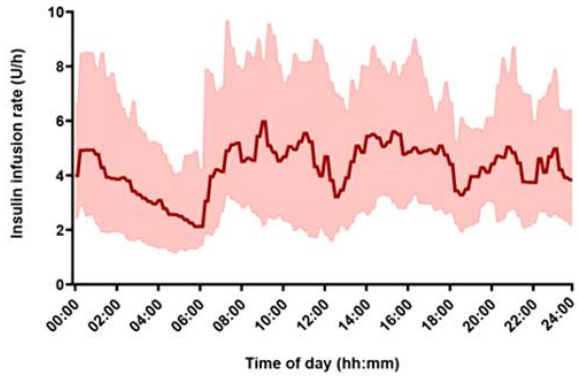
- Additional data on the InRange trial comparing **Toujeo** with **Tresiba** on patients using CGMs, detailed of CGMs data showing a **slightly better GMI for Tresiba** (7.3% vs 7.5%, all with 7.5% at baseline), and a **slightly better TIR** (55.4% vs 52.4%, baseline 51.9% vs 51.2%)
- Additional data of SURMOUNT-1 testing **tirzepatide** in **obese patients** were presented. Data can be found in these slides

Devices

CAMAPS full closed-loop in T2D

- Cross-over, open-label trial testing **CamAPS** in **full closed-loop** mode with **Fiasp** compared to standard insulin therapy during 8 weeks in **n=26 T2D** requiring insulin
  - **Inclusion**: 18 years or over, currently using insulin, A1c < 11%
  - **Baselines**: **59 years**, BMI 35.3 kg/m², **A1c = 9.0%,** 8.5 years on insulin, total insulin dose: 0.70 UI/kg/day, 3 were already on CGM
  - **Results**:
    - **Improved TIR** (70-180mg/dl): **66.3%** ± 14.9 **vs 32.3%** ± 24.7 (p<0.001)
    - **A1c**: **7.3%** ± 0.8 vs **8.7%** ± 1.2 (p<0.001)
    - Time < 70mg/dl: 0.44% vs 0.08%, p=0.43
    - Total daily insulin 108 UI/day vs 84 UI/day
    - 92.3% of time in closed-loop
    - No severe hypos, similar serious adverse events
    - Strong acceptability except a few patients having difficulties with alarms during night

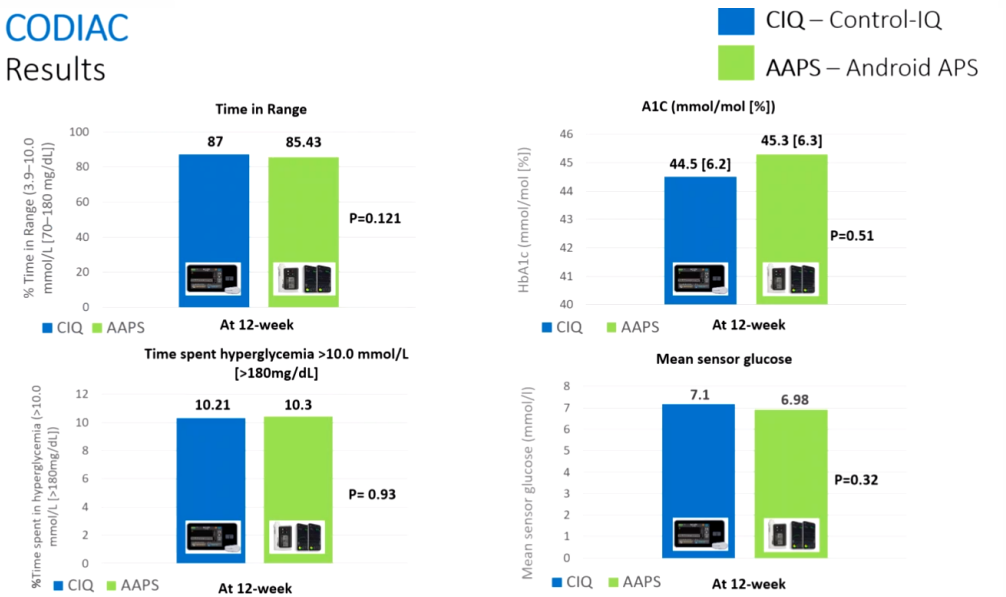




Glucose profiles (in the graph) is rather different than T1D with a much better control during the day than during the night.

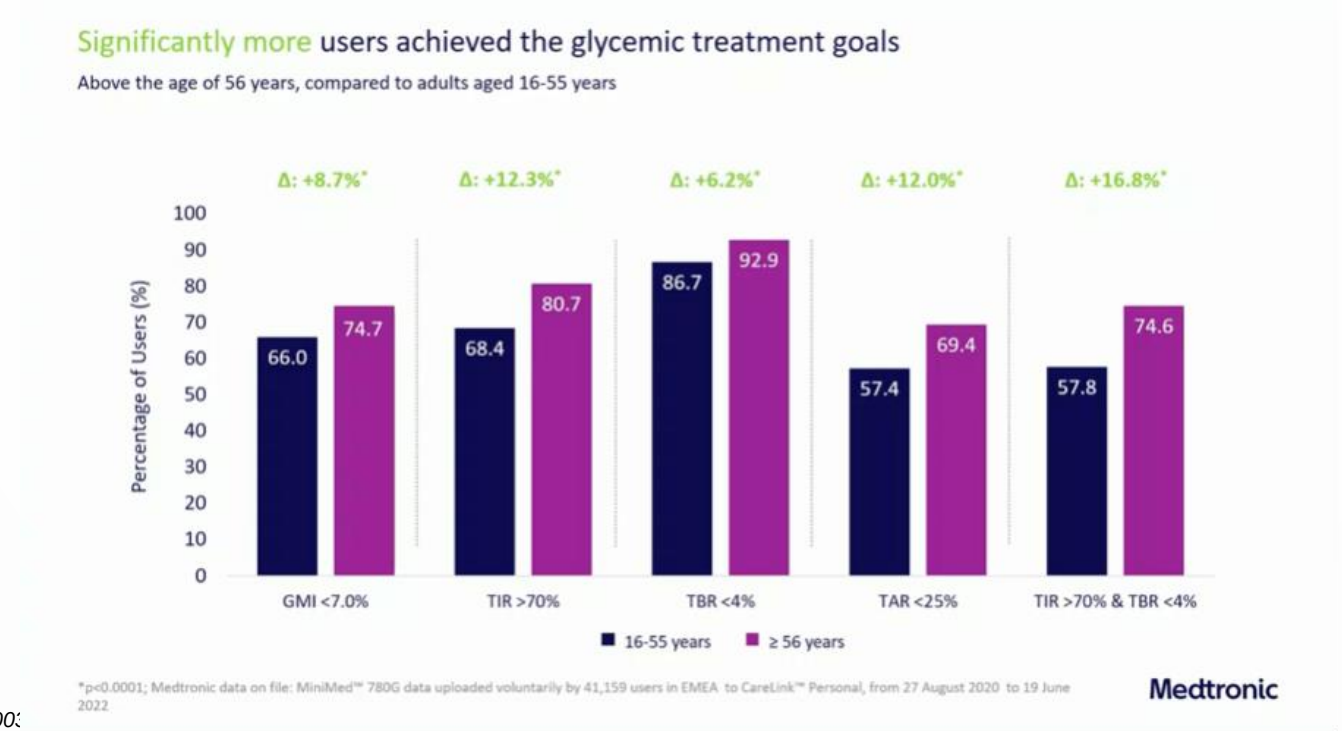
CODIAC study – comparison between control-IQ & Android APS

- CODIAC study comparing **Control-IQ** with **AndroidAPS**
  - Prospective, single arm study testing 1st AndroidAPS for 12 weeks and then Control IQ for 12 weeks (+2 weeks of titration) in **n=23** Czech **adults T1D**
  - **Inclusion**: ≥ 18 years, > 2 years with T1D, using AndroidAPS for at least 3 months
  - **Baselines**: 35.5 years, BMI = 25.1 kg/m², A1c = 6.3%
  - Main results ->
  - Difference time in hypoglycemia statistically significant (p=0.003), 4% with AAPS vs 2.52% with CIQ



Medtronic 780G real-world in older adults

- Real-world data of **European 780G users, aged 56 years or more. N=4,769**
- **TIR of 78% with 81% of patients with TIR > 70%**
  - TIR of 74% in younger adults with 68% with TIR < 70%



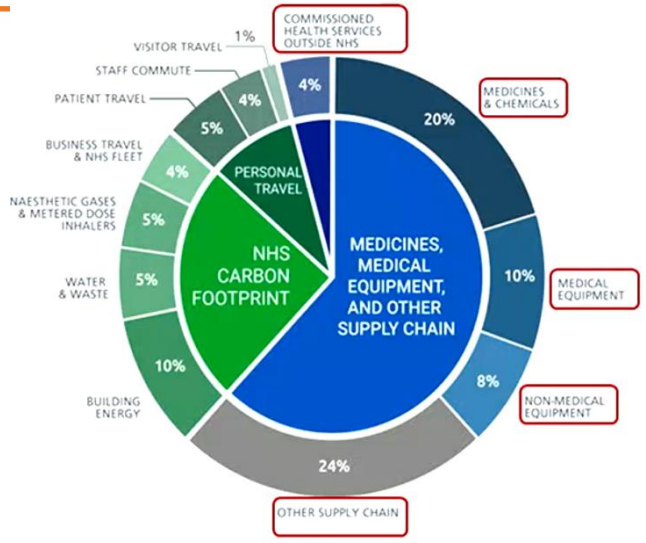
Others in devices

- Dexcom G7 symposium presenting **all features of the Dexcom G7 with accuracy data**, details all type of alerts.
- Long symposium on **Libre that details numerous clinical results of its use**. Pipeline update with **new sensor combining glucose & ketone monitoring**, same design as Libre 3, no calibration, measure of both each minutes, **pivotal to start in 2023**. Launch of CamAPS + Ypsopump + Libre 3 in Germany by end of the year, larger launch in Europe in 2023
- Insulet presented **additional analysis of the pivotal trial for Omnipod 5**
  - Sub analysis of patients that had diabetes for less than a year, similar results as the rest with strong improvement of TIR and slightly higher time in hypo (non sign) while a strong increase was expected due to the end of the honey moon period
  - Follow-up at 15 months, still good glycemic control with slightly higher A1c & lower TIR
- Short presentation on **Tandem PRO data** in **patients with disabilities**. The more patients have disabilities, the less pumps are adapted and so need to be improved. Most of them have vision problems. Digital health can help some of them
- **Tandem Control-IQ real-world results** in n=71,686 users with A1c = 8.2% at baseline to **GMI = 7.2% at 1 year** (but A1c is not exactly the same as GMI)
-

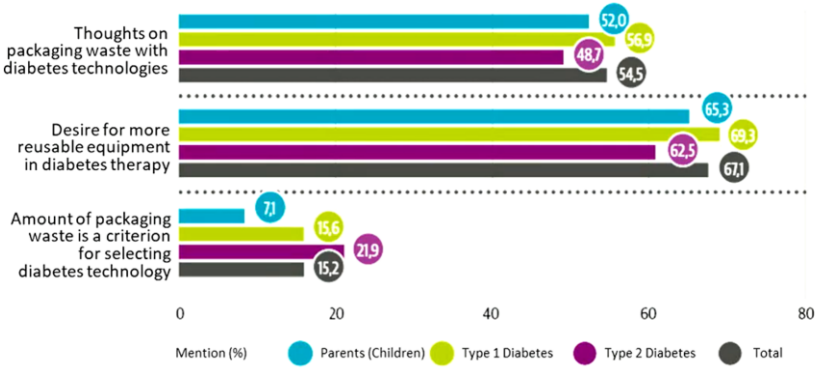
Diabetes and climate change

- **Specific symposium on impact of diabetes and healthcare on climate change.**
- Talk 1 on **NHS** effort in UK on the topic
  - Topic on interest by the NHS that has a special program/team working on a net zero target.
  - Currently they are focusing on measuring carbon impact of different part of the healthcare system (corresponding to more than 4% of the global carbon footprint) -> **guidelines on how to measure carbon footprint**
  - Ongoing pilot in UK to recycle pre-filled pen by Novo (shipped back to Denmark)
  - Her view, carbon impact is at the same point as health economics 20 years ago, **at some point it will be an important factor in the process of reimbursement**
- Talk 2 by **Lutz Heinemman**, detailed wastes coming from medical devices in diabetes with the coming challenges
  - His view: **carbon footprint will be a key parameter for patients to choose their devices, especially wastes produced (packaging, leaflet, boxes…)**

Topic that is getting more and more traction, especially in Europe



Sources of carbon emissions by proportion



Analysis provided by Sam Collaudin

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