Kinexum ATTD 2022 report

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Presentation - disclaimers

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- It synthesizes selected data presented during the ATTD 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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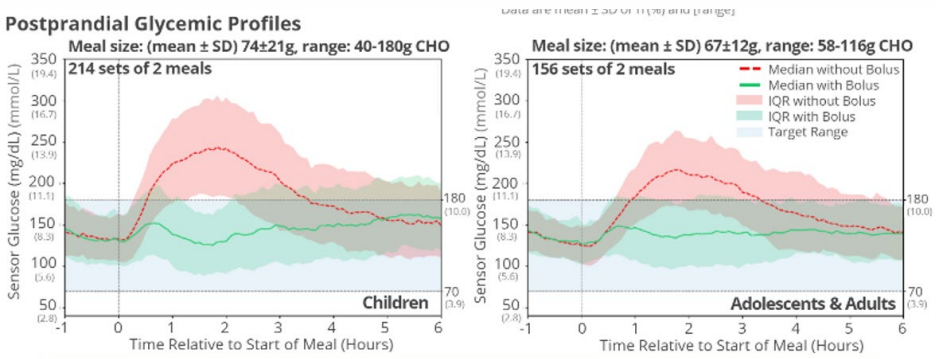
Insulet

- Among Insulet symposium, presentations & posters some new results were presented:
  - Omnipod 5 results in T2D (next slide)
  - Omnipod 5 results in very young children (next slide)
- Poster presenting **meal tests in 6-14 years & 14-70 years T1D** with or without bolus →
- Timelines updates:
  - Limited US commercial launch of Omnipod 5 underway
  - CE mark under review
  - US 2-6 years indication under FDA review
  - Feasibility study in T2D done



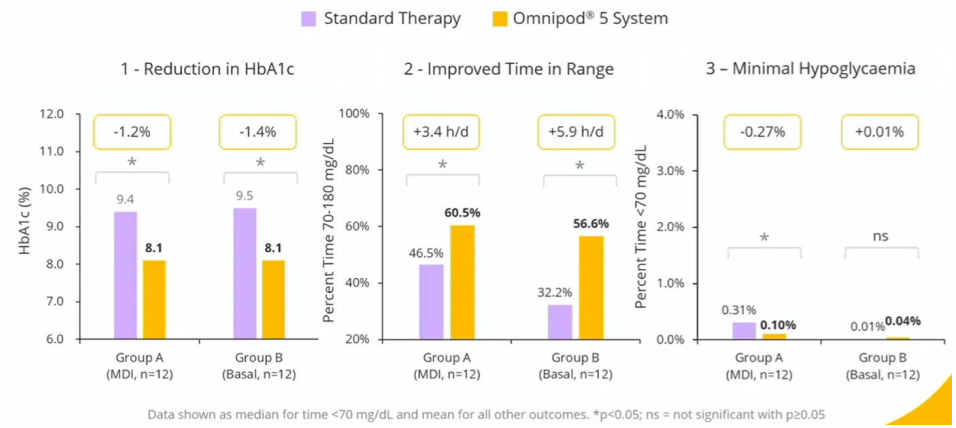
There was no significant difference in mean sensor glucose 6 hours post-meal with vs. without bolus (p≥0.05)

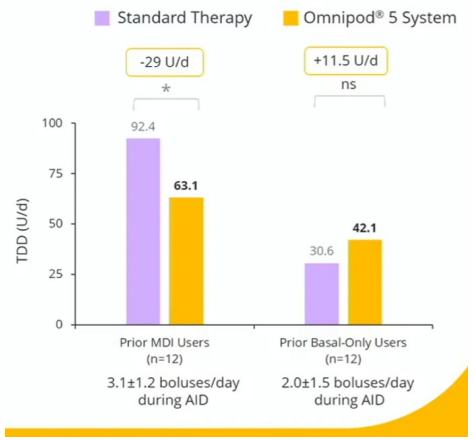
Metrics over the 6h Postprandial Period	Children		Adolescents & Adults	
Pre-Meal Bolus?	With	Without	With	Without
Max CGM value (mg/dL)	238 ± 64	294 ± 63	216 ± 50	263 ± 60
(mmol/L)	13.2 ± 3.6	16.3 ± 3.5	12.0 ± 2.8	14.6 ± 3.3
CGM at 6h post-meal (mg/dL)	164 ± 61	158 ± 60	145 ± 49	153 ± 59
(mmol/L)	9.1 ± 3.4	8.8 ± 3.3	8.1 ± 2.7	8.5 ± 3.3
Area Under the Curve[1] (mg/dL*h)	149 [50, 302]	370 [193, 529]	134 [44, 265]	298 [180, 464]
(mmol/L*h)	8.3 [2.8, 16.8]	20.6 [10.7, 29.4]	7.4 [2.4, 14.7]	16.6 [10.0, 25.8]
Sensor Glucose % Time in Range: % <54mg/dL (3.0mmol/L)	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
% <70mg/dL (3.9mmol/L)	1.4 [0.0, 5.9]	0.0 [0.0, 0.0]	0.0 [0.0, 4.3]	0.0 [0.0, 0.0]
% 70–180mg/dL (3.9–10.0mmol/L)	66.6 ± 25.3	46.1 ± 23.6	72.3 ± 22.7	55.3 ± 25.6
% >180mg/dL (10mmol/L)	29.1 ± 26.4	52.1 ± 24.3	24.1 ± 23.4	43.3 ± 26.0
% >250mg/dL (13.9mmol/L)	0.0 [0.0, 13.4]	18.4 [0.0, 36.8]	0.0 [0.0, 0.0]	4.2 [0.0, 24.5]
% >300mg/dL (16.7mmol/L)	0.0 [0.0, 0.0]	0.0 [0.0, 18.6]	0.0 [0.0, 0.0]	0.0 [0.0, 2.6]
Time in Automated Mode (%)	97.2 [88.9, 100]	95.8 [84.7, 100]	100 [90.3, 100]	100 [93.1, 100]
Automated Insulin Delivery (U)	4.1 ± 3.0	6.5 ± 4.0	4.9 ± 2.8	7.3 ± 3.8
Total Insulin Delivery[2] (U)	14.1 ± 7.7	10.5 ± 6.6	15.8 ± 6.9	14.0 ± 6.8

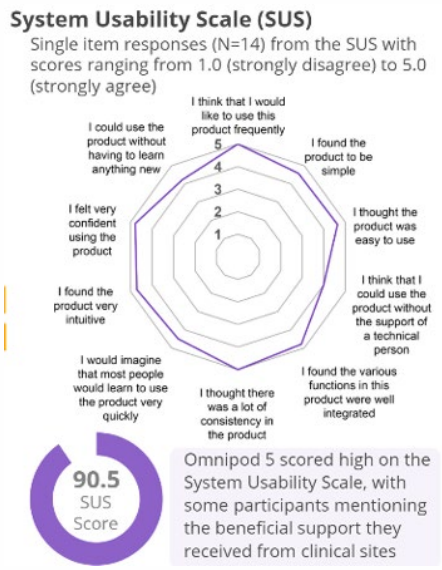
Data are mean ± SD or median [IQR] [1]Defined as area below the glucose curve but above 180mg/dL (10 mmol/L) [2]Includes pre meal bolus if given

Insulet – Omnipod 5 in T2D

- Single-arm outpatient study testing Omnipod 5 in n=24 **adults** (18-75 years) **T2D** during 8 weeks
- Inclusion criteria: A1c 8-12%, MDI (12 basal only, 12 basal-bolus), CGM users or naïve, max 200UI/day
  - Group A, basal bolus patients: 4 weeks with optional boluses followed by 4 weeks with simplified boluses
  - Group B, basal only: 4 weeks with optional boluses followed by 4 weeks with simplified boluses if TIR ≤ 50%, optional boluses if > 50%
- Baselines: Age = 62 & 59 years, BMI = 35.2 & 31.9 kg/m², **54% CGM naïve**
- Results: **A1c** reduced from **9.4% to 8.1%, TIR** improved from **39.3% to 58.6%**, time < 70mg/dl reduced from 0.13% to 0.06%, all p<0.05
- Insulin delivery satisfaction survey (**IDSS**), **improved from 3.5 to 4.2**, p<0.05

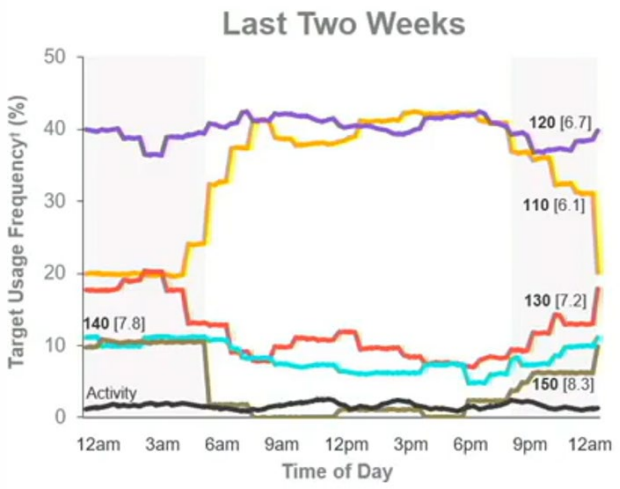


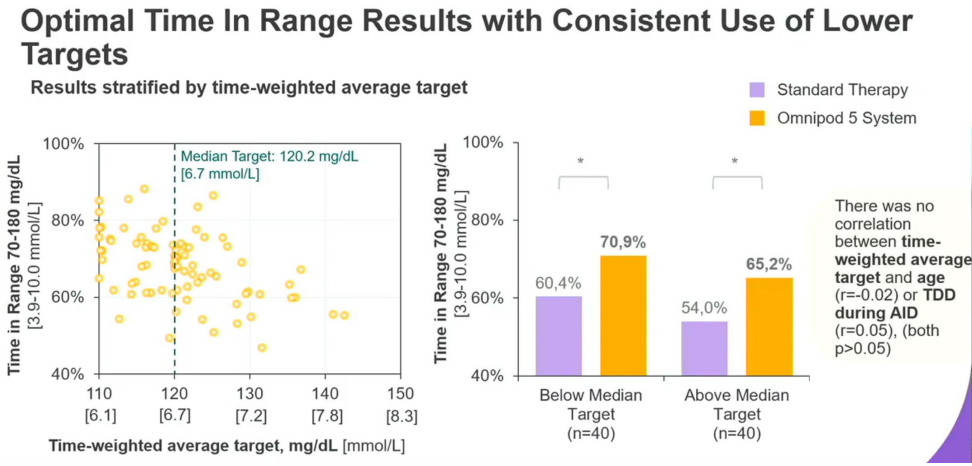




Insulet – Omnipod 5 in very young children

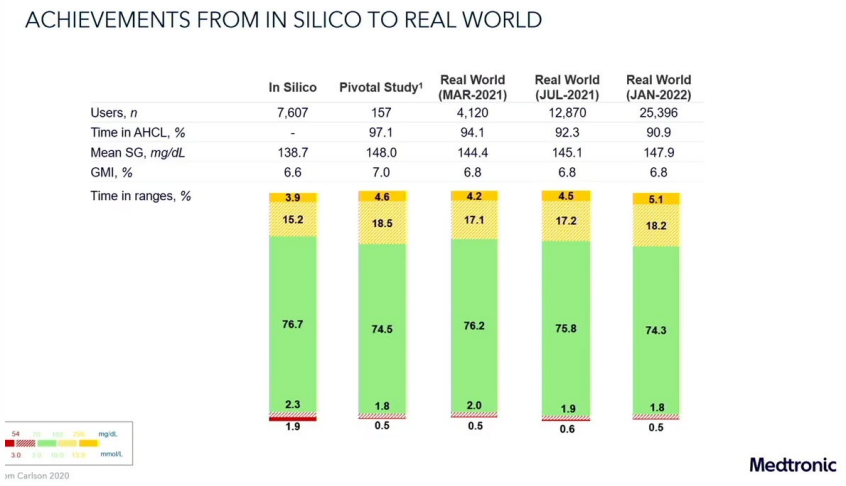
- Single-arm outpatient study testing **Omnipod 5** in n=80 very young T1D (**≥ 2 years & < 6 years**) during 8 weeks
- Inclusion criteria: A1c < 10%, no severe hypos or DKA during past 6 months
- Baselines: Age = 4.7 years, 20% between 2 & 4 years, weight = 19.7 kg, **7.4% A1c**, **13.7 UI/day**, 15% MDI
- 35% of children mostly use the 110mg/dl target, 41% the 120mg/dl
- Results: **TIR improved from 57.2% to 68.1%,** time < 70mg/dl reduced from 2.2% to 1.9% (p<0.05)
- All user experience index presented were significatively improved, **IDSS from 3.9 to 4.3**, treatment satisfaction by 23.9…





Medtronic - 780G real-world data

- Medtronic presented **real-world data** based on data gathered through CareLink
- Previous data with lower number of patients (and possibly highly motivated ones) were slightly better than pivotal trials. Recent one on a larger population show results that correspond almost exactly to the pivotal trial
- Disparities are seen in between countries (as previously presented with the 670G, probably diet, culture & education impacts)
- TIR results depends on parameters with higher time in range with aggressive parameters (up to 80.7%) but with higher time below 70 mg/dl (2.9%)



Users, *n*		Active Insulin Time (≥95% of the time)				
		2 Hours	2-3 Hours	3-4 Hours	>4 Hours	Total
Glucose Target (≥95% of the time)	100 mg/dL	1,482	1,448	177	7	3,316
	110 mg/dL	306	707	120	2	1,183
	120 mg/dL	289	764	129	3	1,254
	Total	4,507	6,172	954	32	12,870

TIR (70-180 mg/dL), %		Active Insulin Time (≥95% of the time)				
		2 Hours	2-3 Hours	3-4 Hours	>4 Hours	Total
Glucose Target (≥95% of the time)	100 mg/dL	80.7	78.2	75.0	76.8	79.3
	110 mg/dL	77.4	75.3	75.3	64.4	75.9
	120 mg/dL	74.6	73.2	69.9	68.7	73.2
	Total	77.8	74.8	72.4	70.1	75.8

GMI, %		Active Insulin Time (≥95% of the time)				
		2 Hours	2-3 Hours	3-4 Hours	>4 Hours	Total
Glucose Target (≥95% of the time)	100 mg/dL	6.6	6.7	6.8	6.8	6.6
	110 mg/dL	6.8	6.8	6.8	7.2	6.8
	120 mg/dL	6.9	7.0	7.1	6.8	7.0
	Total	6.7	6.8	6.9	7.0	6.8

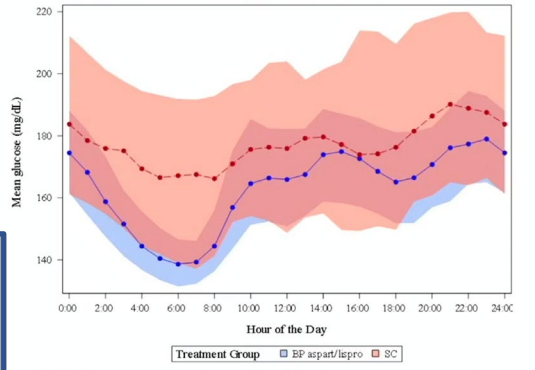
TBR (<70 mg/dL), %		Active Insulin Time (≥95% of the time)				
		2 Hours	2-3 Hours	3-4 Hours	>4 Hours	Total
Glucose Target (≥95% of the time)	100 mg/dL	2.9	2.6	2.6	1.7	2.8
	110 mg/dL	2.2	2.1	2.0	1.4	2.1
	120 mg/dL	1.9	1.7	1.5	6.1	1.8
	Total	2.7	2.3	2.2	2.5	2.5

Beta bionics - insulin only pivotal trial

- Pivotal trial testing the **iLet** with either **Lispro/Aspart** (BP A/L) either **Fiasp** (BP F) compared to **standard of care** (SC, current treatment that can be insulin pump, HCL or MDI), in **n=440 children** (6-18 years) or **adults** with **T1D** during 13 weeks
- Inclusion criteria: use of CGM or at least 3 BGM tests/day
- Baselines:
  - 89% using CGM
  - 34% MDI
  - 31% with HCL (23% with control-IQ)

Long awaited results of BB single hormones. Results are similar to other HCL system Dual-hormone pivotal ongoing.

Mean Glucose by Hour of the Day

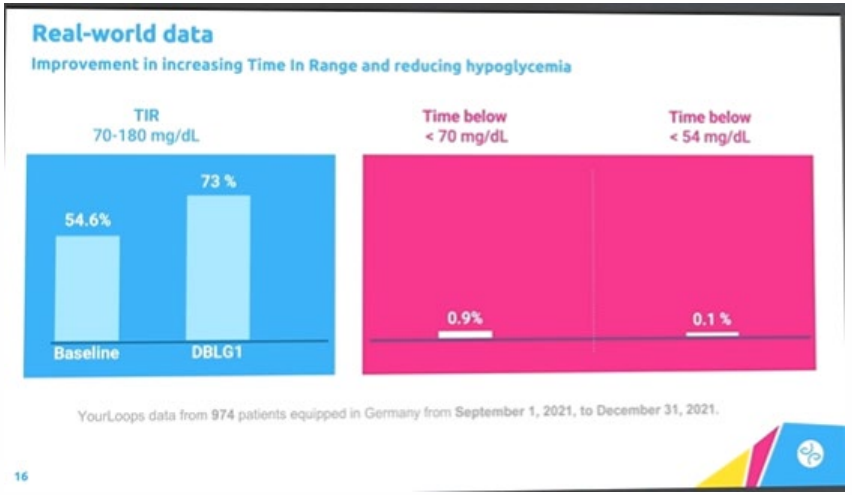


Solid dots represent medians, colored bands represent interquartile ranges

	All population		Children (6-18 years)		Adults			Patients with A1c > 7%	
Treatment	SC n=107	BP A/L n=219	SC n=53	BP A/L n=112	SC n=54	BP A/L n=107	BP F n=114	SC n=76	BP A/L n=164
Baseline A1c	7.7%	7.9%	7.7%	7.9%	7.6%	7.6%		8.2%	8.3%
A1c at 13 weeks	7.7%	7.3%	7.7%	7.3%	7.5%	7.1%		8.1%	7.5%
Baseline adjusted group difference		-0.5%*		-0.5%*		-0.5%*			-0.7%*
Baseline median time < 54 mg/dl	0.20%	0.21%							
median time < 54 mg/dl at week 13	0.24%	0.33%							
Baseline adjusted group difference		0.00%		0.02% p=0.33		-0.04% p=0.24%			
Mean TIR at week 13	**54%**	**65%***	**50%**	**60%***	**58%**	**69%***	**71%***		
Severe hypo events per 100 person years	10.8	17.7			14.2	10.2			

Diabeloop

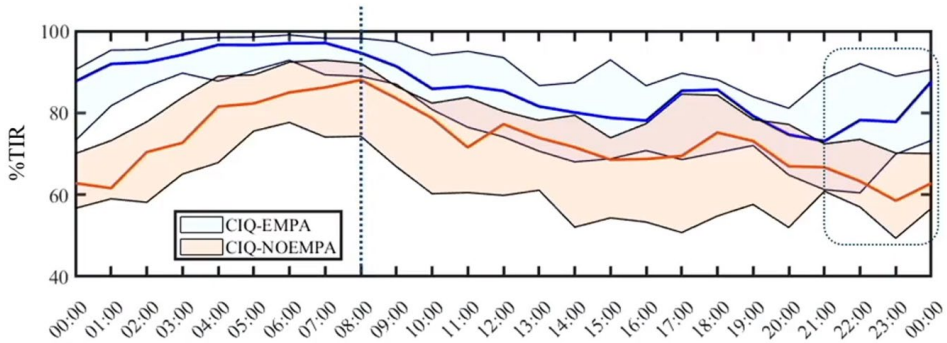
- First real-world data showing better glucose control than during the pivotal trial **(+18.4% TIR vs 12%)** →
  - **These data correspond to the first users, usually highly motivated by using this new technology, that could be an explanation for these better results, could be less good in the future**
- Ongoing projects
  - algorithm improvements (unannounced meals, self-learning…
  - indication extension (underserved population, children, teens, other insulins, T2D with a fully automated mode…)
  - integration with smart pen
  - integration of smart watch data (heart rate, accelerometer) in their algorithm
- They currently have **7,000 users in Europe**
- Poster with positive reduction of time in hypo for T1D patients with more than 5% of time in hypos at baseline →→→



WP7 (n=9)		WP8 (n=28)		WP9 (n=8)		Total (n=45)	
OL	CL	OL	CL	OL	CL	OL	CL
Diff CL - OL p-value		Diff CL - OL p-value		Diff CL - OL p-value		Diff CL - OL p-value	
Time Below Range 70 mg/dL							
8.30 ±2.34	3.31 ±1.62	7.9 ±2.53	3.08 ±1.67	7.43 ±2.12	3.46 ±1.7	**7.9 ±2.39**	**3.2 ±1.63**
-5.88 [-6.83, -3.14] 0.0003		-4.85 [-5.59, -4.04] $<10^{-4}$		-3.99 [-5.29, -2.66] 0.0002		**-4.73** [-5.3, -4.1] $<10^{-4}$	
Time Below Range 54 mg/dL							
2.1 ±1.05	0.78 ±0.49	1.9 ±1.5	0.73 ±0.84	1.59 ±0.85	0.88 ±0.62	**1.89 ±1.31**	**0.77 ±0.74**
-1.27 [-2.1, -0.54] 0.0044		-0.88 [-1.55, -0.79] $<10^{-4}$		-0.6 [-1.12, -0.3] 0.0047		**-0.89** [-1.39, -0.84] $<10^{-4}$	
Time In Range 70-180 mg/dL							
65.38 ±9.35	71.95 ±10.63	62.48 ±10.27	67.38 ±8.17	63.56 ±6.78	66.76 ±3.76	**63.25 ±9.45**	**68.19 ±8.21**
6 [2.4, 10.74] 0.0066		4.71 [1.84, 7.96] 0.0028		4.24 [-0.72, 7.12] 0.0944		**5.11** [2.85, 7.02] $<10^{-4}$	

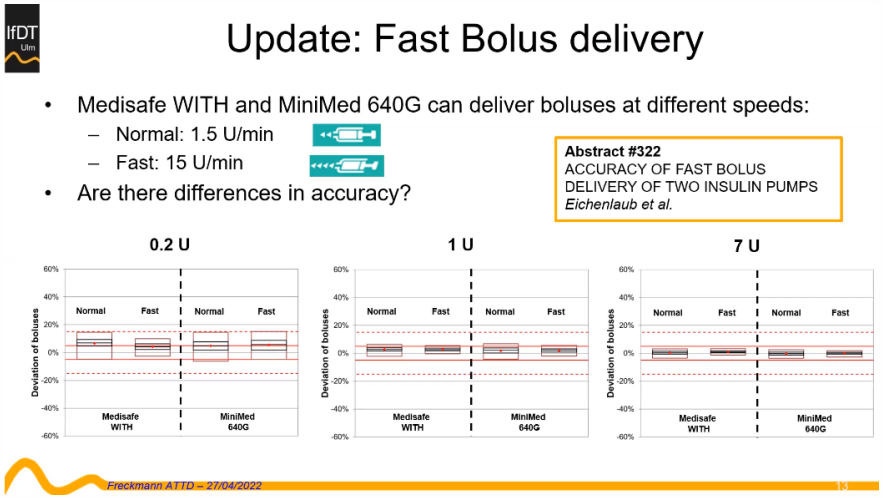
Control-IQ and SGLT-2i in T1D

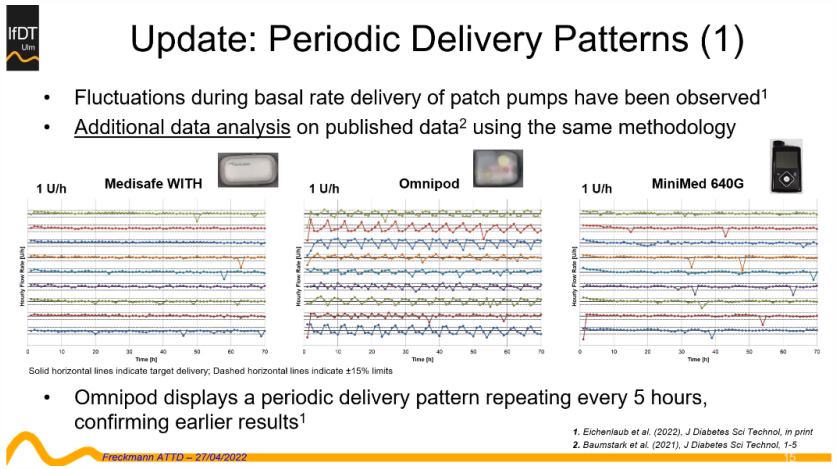
- Crossover trial testing **Control-IQ** 4 weeks followed by Basal-IQ 2 weeks and Basal-IQ 2 weeks + Control-IQ 4 weeks **with or without 5mg empagliflozin** in n=35 T1D
- Inclusion: 18-65 years, using insulin pump, A1c ≤ 9%, no history of DKA or severe hypo in the past 12 months
- Baselines: 41 years, BMI=29 kg/m², **A1c=6.8%**
- Results:
  - **81% TIR vs 71% (p=0.04)**
  - 1.1% vs 1.9% time < 70mg/dl (p=0.2)
  - 1 episode of DKA leading to discontinuation
- Corresponding publication



Terumo Patch pump accuracy

- Terumo presented results (own data) with similar accuracy as Medtronic pumps and with lower accuracy at low volumes (Data published and previously presented). They presented additional data on accuracy depending on speed of injection vs the 640G (similar results) and on periodic patterns.





Sigi Patch pump

- Short presentation at the FAIR of new technologies and some accuracy data presented in a poster

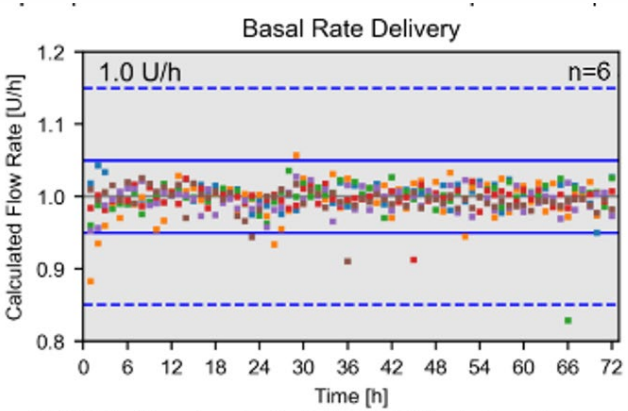


FIGURE 1: Mean basal rate delivery of 1-h-windows (colored squares) for a basal rate of 1.0 U/h (n=430). Dashed blue lines: ±15%-range; solid blue lines: ±5%-range.

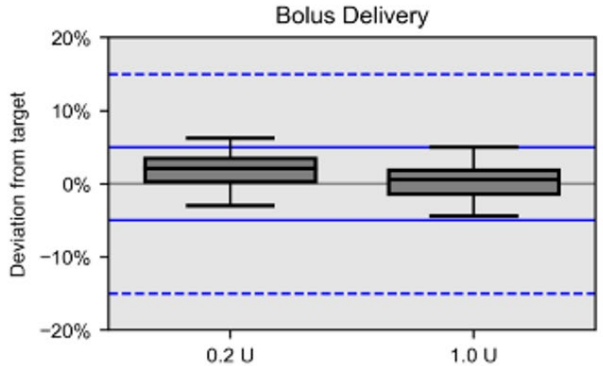


FIGURE 2: Bolus accuracy for 0.2 U (left) and 1.0 U (right) boluses. Horizontal lines, boxes and antennae indicate median, 50% and 95% of values, respectively (n=150). Dashed blue lines: ±15%-range; solid blue lines: ±5%-range.

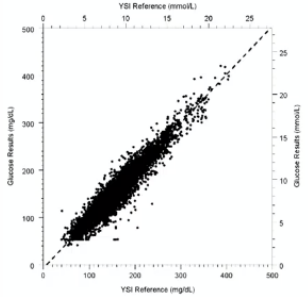
Abbott – Libre freestyle 3 accuracy trial

- Abbott presented the results of their accuracy trial with the **Libre Freestyle 3** in n**=100 4 years and older T1D or T2D**
- **MARD of 7.8%**
- 93.4% of readings within ± 20% if ≥ 70 mg/dl, 93.3% of readings within ± 20 mg/dl if < 70 mg/dl

FREESTYLE LIBRE 3 ACCURACY STUDY

FreeStyle Libre 3 performance

FreeStyle Libre 3 system current glucose versus YSI



Parameter	Value
Slope	1.03
Intercept	-8.1 mg/dL (-0.45 mmol/L)
Correlation	0.96
N	6845
Range	40-405 mg/dL (2.2-22.5 mmol/L)
Overall mean bias	-3.7 mg/dL (-0.2 mmol/L)
MARD	7.8%

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YSI: Yellow Spring Instrument YSI 2300

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FREESTYLE LIBRE 3 ACCURACY STUDY

FreeStyle Libre 3 performance with glucose level

Glucose level	MAD	MARD
<54 mg/dL (3.0 mmol/L)	16.5 mg/dL (0.9 mmol/L)	
54-69 mg/dL (3.0-3.8 mmol/L)	8.0 mg/dL (0.4 mmol/L)	
70-180 mg/dL (3.9-10.0 mmol/L)		8.4%
181-250 mg/dL (10.0- 13.9 mmol/L)		6.3%
251-350 mg/dL (13.9-19.4 mmol/L))		4.9%
>350 mg/dL (19.4 mmol/L)		4.1%

MAD, Mean absolute difference is provided for glucose levels <70 mg/dL; MARD, mean absolute relative difference is provided for glucose levels ≥70 mg/dL.

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Dexcom – G7 accuracy data

- Dexcom presented the results of their accuracy trial testing their **G7 CGM in n=316 T1D & T2D adults** & **n=164 T1D pediatrics** (2-17 years)
- Results synthetized in the tables →
- Adults publication
- Paediatrics publication

G7 Accuracy Across CGM Glucose Ranges: Adult Arm Wear (N=308)

Glucose Range mg/dL (mmol/L)	Matched Pairs (N)	%15/15 mg/dL	%20/20 mg/dL	MARD (%)	MAD (mg/dL)
40-60 (2.2-3.3)	2,444	**85.1**	**91.9**	NA	8.5
61-80 (3.4-4.4)	5,485	**92.6**	**96.5**	NA	6.3
81-180 (4.5-10)	15,319	86.2	93.6	8.9	N.A.
181-300 (10.1-16.7)	10,465	90.3	96.0	7.2	N.A.
301-400 (16.8-22.2)	5,480	96.8	99.1	5.4	N.A.

MARD: presented for CGM values > 80 mg/dL (4.4 mmol/L)
MAD: presented for CGM values ≤ 80 mg/dL (4.4 mmol/L)
Percent 15/15: proportion of CGM values that were within 15% of paired YSI values >100 mg/dL (5.6 mmol/L) or 15 mg/dL (0.8 mmol/L) of YSI values ≤100 mg/dL (5.6 mmol/L)
Percent 20/20: proportion of CGM values that were within 20% of paired YSI values >100 mg/dL (5.6 mmol/L) or 20 mg/dL (1.1 mmol/L) of YSI values ≤ 100 mg/dL (5.6 mmol/L)
Garg, S.et al. Diabetes Technology & Therapeutics. Ahead of print. http://doi.org/10.1089/dia.2022.0011.

Dexcom G7 Provided Accurate Sensor Glucose Readings in Pediatric Participants with T1D

In 7-17 year olds

Arm-placed sensors
Overall MARD: **8.1%**
Overall %20/20: **95.3%**

Abdomen-placed sensors
Overall MARD: **9.0%**
Overall %20/20: **92.9%**

In 2-6 year olds
Overall MARD: **9.3%**
Overall %20/20: **91.5%**

Pediatric Arm Wear Accuracy across CGM Glucose Ranges in 7-17 year olds (N=122)

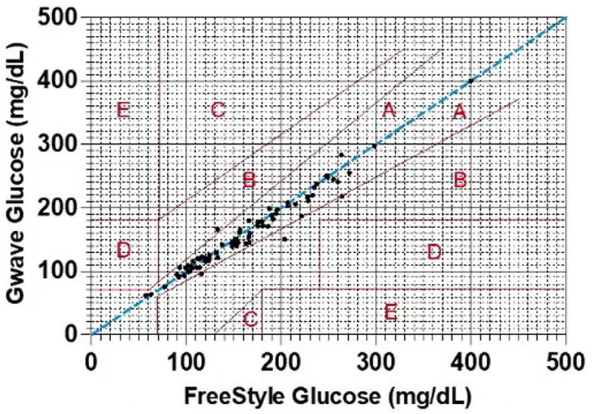
Glucose Range mg/dL (mmol/L)	Matched Pairs (N)	%15/15 mg/dL	%20/20 mg/dL	MARD (%)	MAD (mg/dL)
40-60 (2.2-3.3)	402	74.4	85.3	NA	11.3
61-80 (3.4-4.4)	1,089	93.0	95.5	NA	6.4
81-180 (4.5-10)	3,386	86.5	94.1	8.4	N.A.
181-300 (10.1-16.6)	2,029	88.5	97.0	7.6	N.A.
301-400 (16.7-22.2)	1,162	96.9	99.4	5.4	N.A.

MARD: presented for CGM values > 80 mg/dL (4.4 mmol/L)
MAD: presented for CGM values ≤ 80 mg/dL (4.4 mmol/L)
Percent 15/15: proportion of CGM values that were within 15% of paired YSI values >100 mg/dL (5.6 mmol/L) or 15 mg/dL (0.8 mmol/L) of YSI values ≤100 mg/dL (5.6 mmol/L)
Percent 20/20: proportion of CGM values that were within 20% of paired YSI values >100 mg/dL (5.6 mmol/L) or 20 mg/dL (1.1 mmol/L) of YSI values ≤ 100 mg/dL (5.6 mmol/L)

Gwave CGM

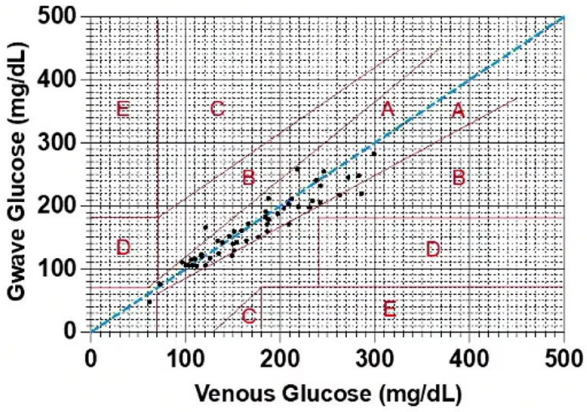
- Non-invasive CGM that should be integrated into a watch, have FDA breakthrough status
- Clinical trial in n=23 subjects, 100% of readings in the A zone on a Clark Error Grid
- Ongoing clinical trial in n=250 T1D & T2D
- Aggregate clinical data to date (68 comparisons to reference lab and/or standard glucometer readings during either a glucose tolerance test or fruit juice challenge) →

Gwave-FreeStyle correlation Overlayed on a Clarke Error Grid



97% A Zone

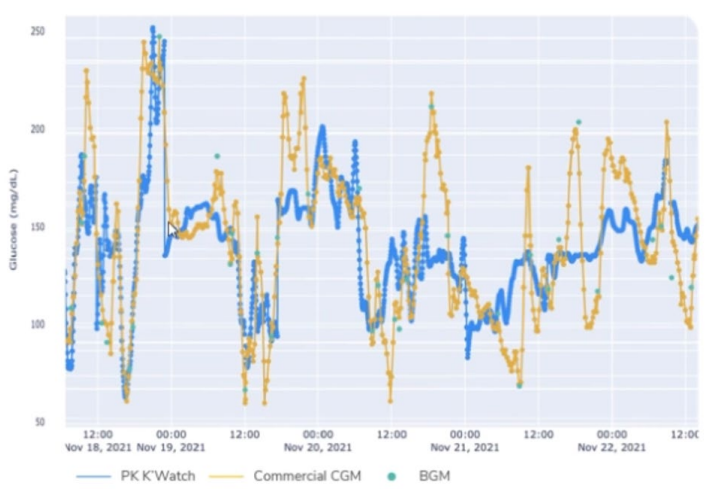
Gwave-Venous correlation Overlayed on a Clarke Error Grid



96% A Zone

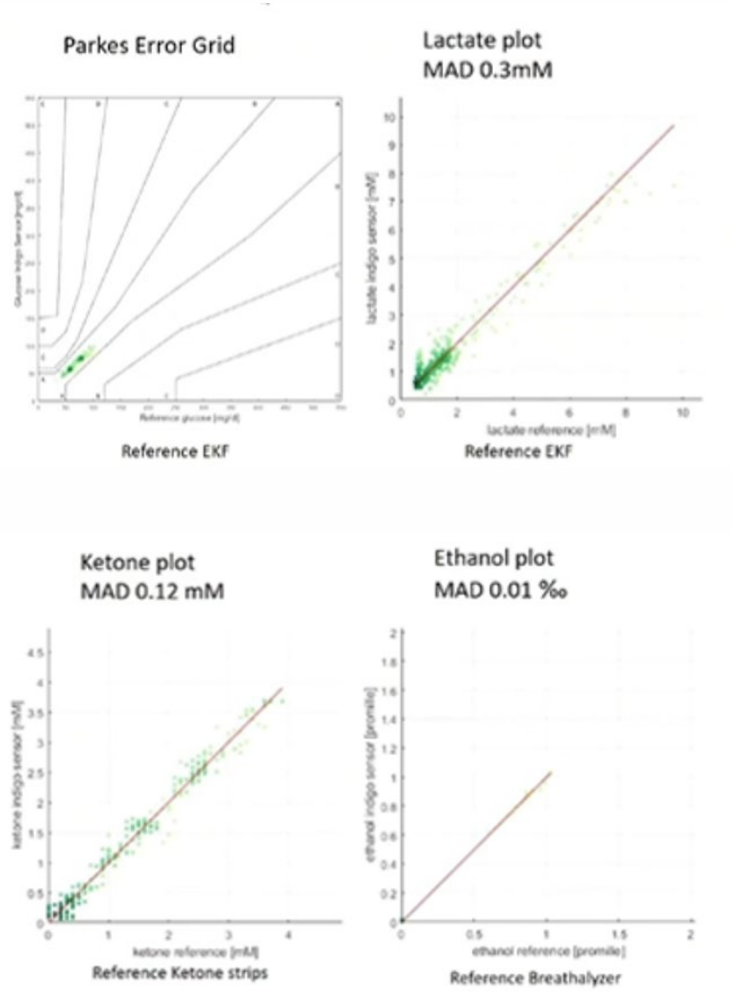
K'Watch from PKVitality

- Watch with a sensor with microneedles (painless). The sensor part (K'apsul) needs to be changed every week.
- Feasibility clinical trial ongoing with 35 patients, first patients show a MARD of 18% with calibration.



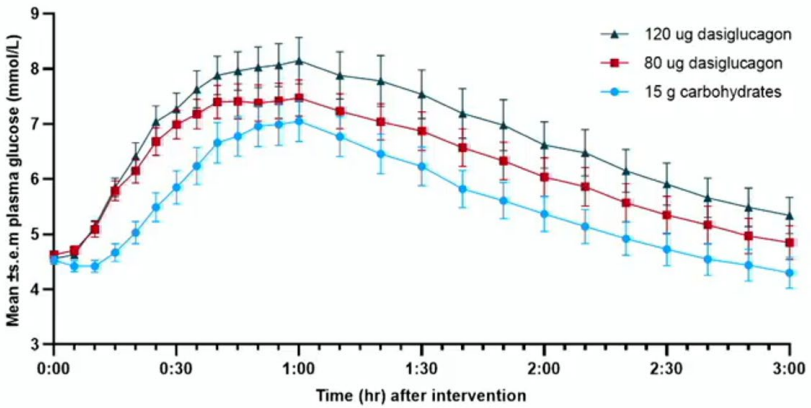
Indigo implantable mutlibiomarker sensor

- Indigo is an implantable multibiomarker sensor that is under development and that can measure blood glucose, ketones, lactate & alcohol
- Results of the GLOW study testing Indigo device in 4 T1D & 3 healthy volunteers
- 1 giant cell foreign body reaction and 1 sensor failure
- Overall glucose MARD of 7.1%, 98.9% in A of the Parkes Error Grid
- MAD of 0.12mM for ketones
- MAD of 0.16mM for lactate



Zealand – dasiglucagon micro-doses

- Results of a crossover, partially blinded, Phase 2 trial testing **80 & 120µg micro-doses** of dasiglucagon vs oral 15g carbohydrates in **n=20 adults T1D** (10 MDI, 10 CSII) with A1c ≤ 8%
- Rescue after an insulin dose aimed to bring PG to 54 mg/dL, intervention when this target is reached
- Results:
  - Faster glucose increase with dasiglucagon than with carb →
  - Results of other trials were presented
  - They presented potential limitations of the use of glucagon →

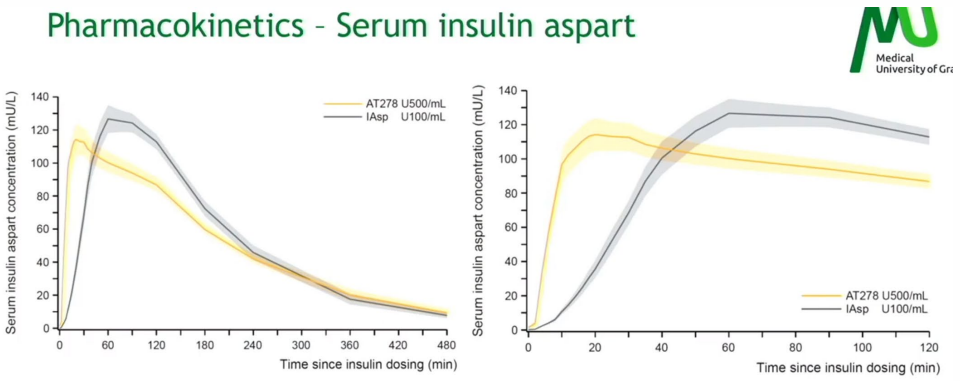


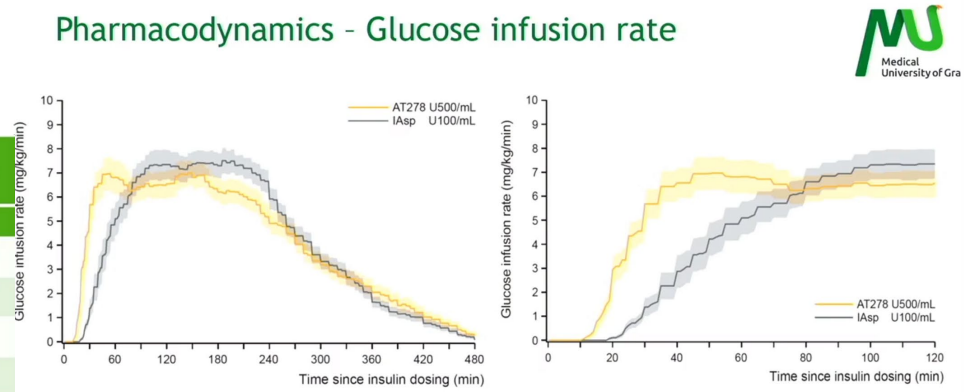
Potential limitations

NO/NO	Glucose level/fall rate of glucose
YES	Ambient insulin levels
NO	Repeated glucagon doses
YES	Low-carbohydrate diet
NO	Exercise
YES	Alcohol
NO	Influence on CGM accuracy
YES	Short term side effects
???	**Cost**

Arecor – AT278 URI concentrated (500UI/ml)

- Single-dose, crossover, double-blind, glucose clamp, FIH trial testing **AT278 (500UI/ml URI)** vs Novorapid in n=38 adults T1D
- Baselines: 38.8 years, 86.4 kg, A1c=7%
- Main results:



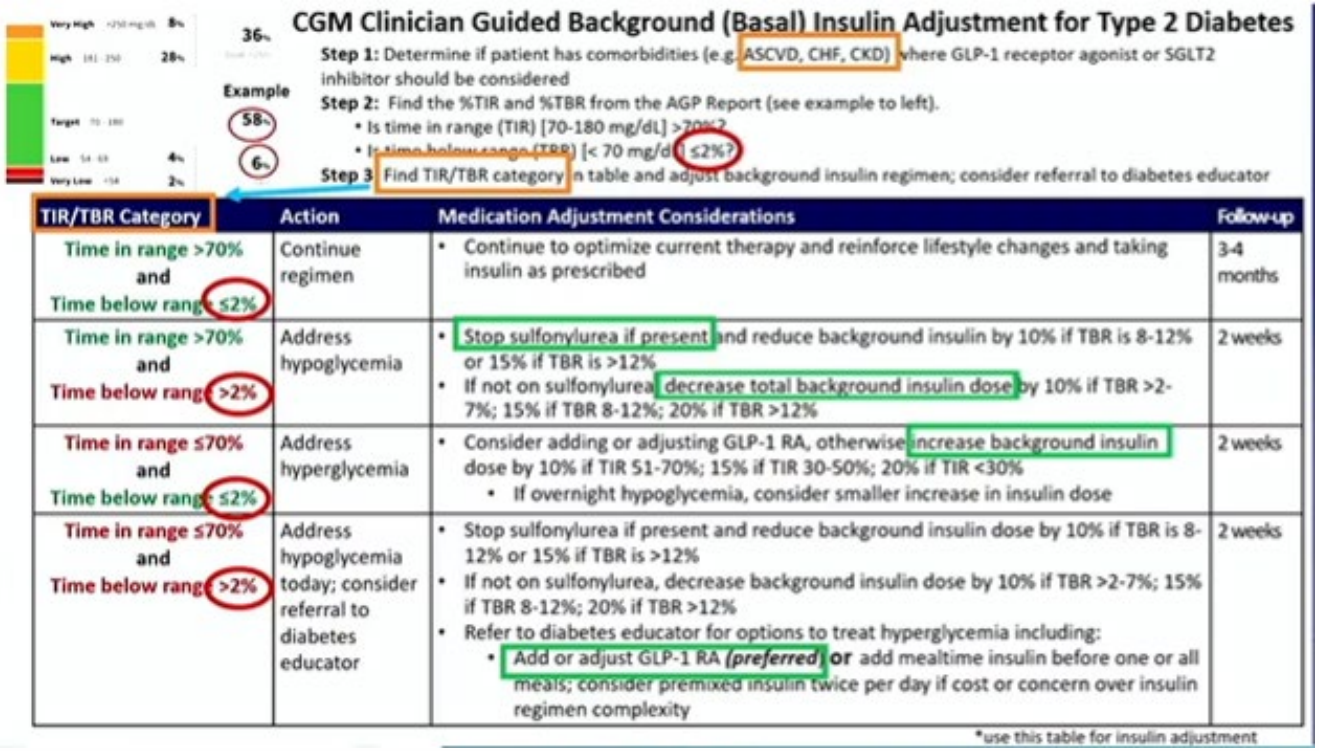


	AT278 n = 38	IAsp n = 38	Treatment difference / ratio (95% CI)	*p*-value
Insulin exposure				
Onset of appearance (min)	3 (3; 4)	9.5 (8; 14)	-6 (-8; -6)	<0.0001
$t_{Early50\%Cmax}$ (min)	7.5 (6; 10)	32 (27; 35)	-23 (-26; -22)	<0.0001
$AUC_{IAsp,0\text{-}30min}$	4 920 (3 160; 7 062)	1 299 (630; 1 975)	**4.02 * (3.29; 4.90)**	
$AUC_{IAsp,0\text{-}60min}$	10 576 (7 766; 14 735)	6 942 (4 369; 9 237)	**1.54 * (1.35; 1.76)**	
Glucose-lowering effect				
Onset of action (min)	11.5 (9; 16)	21.5 (14; 27)	-9.5 (-13; -6)	<0.0001
$t_{Early50\%GIRmax}$ (min)	30 (25; 45)	60 (45; 75)	-20 (-30; -15)	<0.0001
$AUC_{GIR,0\text{-}30min}$	45 ± 42	5 ± 9	**8.91 * (5.96; 17.46)**	
$AUC_{GIR,0\text{-}60min}$	241 ± 157	102 ± 117	**2.36 * (1.92; 3.22)**	

Data are presented as median (25%; 75%) or mean ± SD; *** Treatment ratio (95% CI)** is calculated for AUC variables only

How to best use CGMs to treat T2D

- Talk from Richard Bergenstal on how to use CGMs as a tool to make easy decisions on how to treat T2D patients
- Presented an algorithm based on TIR and TBR →
- Suggest that targeted TIR should be ≥ 70% and TBR ≤ 2% in T2D



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