

Effect of CagriSema on continuous glucose monitoring in people with inadequately controlled type 2 diabetes: REIMAGINE 2

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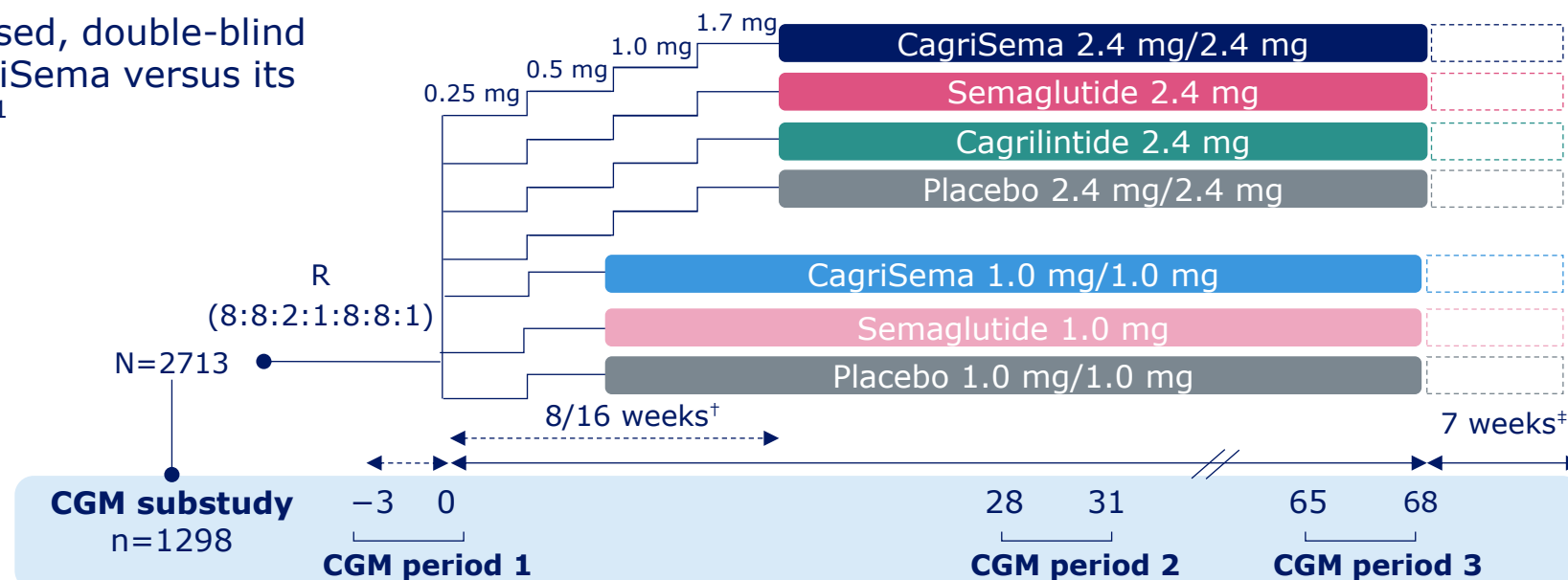
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REIMAGINE 2 was a randomised, double-blind within dose level study of CagriSema versus its monocomponents and placebo¹

Key inclusion criteria

- ≥18 years
- T2D uncontrolled on stable metformin ± SGLT2i
- HbA_{1c} 7.0–10.5%
- BMI ≥25 kg/m²

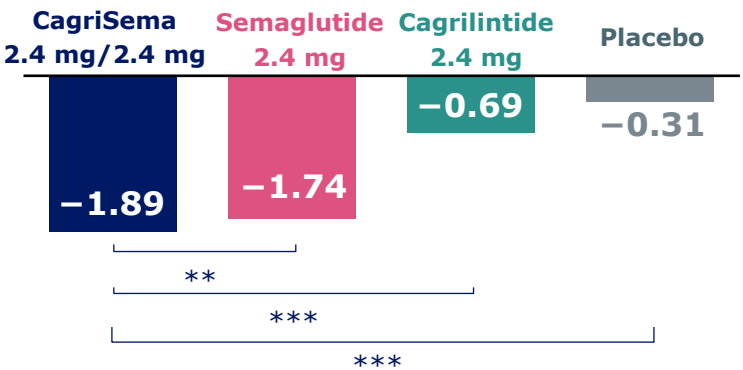


Only CagriSema 2.4 mg/2.4 mg, semaglutide 2.4 mg, cagrilintide 2.4 mg and pooled placebo data have been included in this presentation. [†]Escalation period; [‡]Follow-up period. BMI, body mass index; CGM, continuous glucose monitoring; HbA_{1c}, glycated haemoglobin; R, randomisation; SGLT2i, sodium–glucose cotransporter-2 inhibitor; T2D, type 2 diabetes. 1. Buse JB et al. *Lancet Diabetes Endocrinol* 2026;14:662–677.

Changes in HbA_{1c}, body weight, TIR and TITR (CGM subgroup)

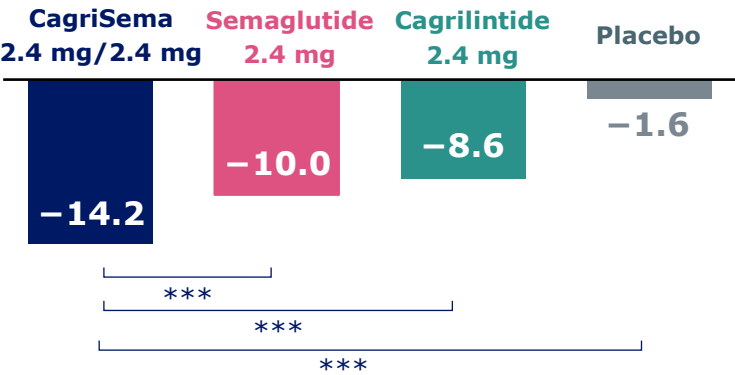
HbA_{1c} (%-points)

Mean at baseline: 8.2%

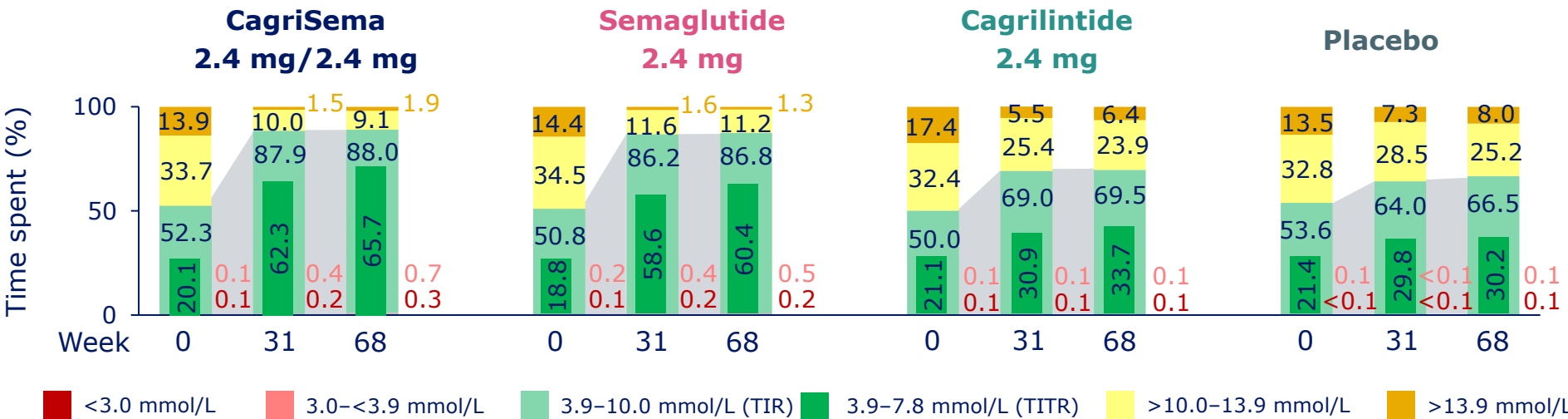


Body weight (%)

Mean at baseline: 102.4 kg



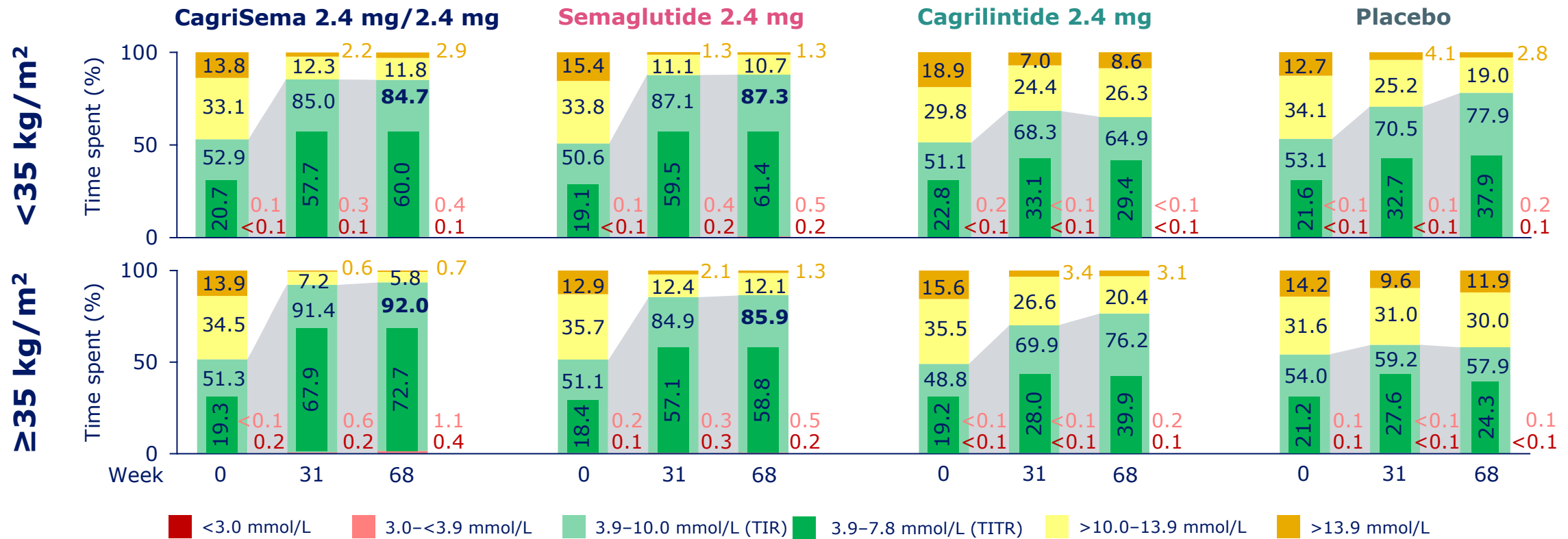
In the CGM subgroup (n=1298), reductions in HbA_{1c} and body weight were greater with CagriSema 2.4 mg/2.4 mg vs its monocomponents



TIR and TITR improved with CagriSema 2.4 mg/2.4 mg and its monocomponents by week 31

Data are estimated mean changes in HbA_{1c} and body weight according to the efficacy estimand, and mean percentage of observed time spent at various glucose ranges for the on-treatment period. p values are not adjusted for multiplicity. **p=0.05; ***p<0.0001. CGM, continuous glucose monitoring; HbA_{1c}, glycated haemoglobin; TIR, time in range; TITR, time in tight range.

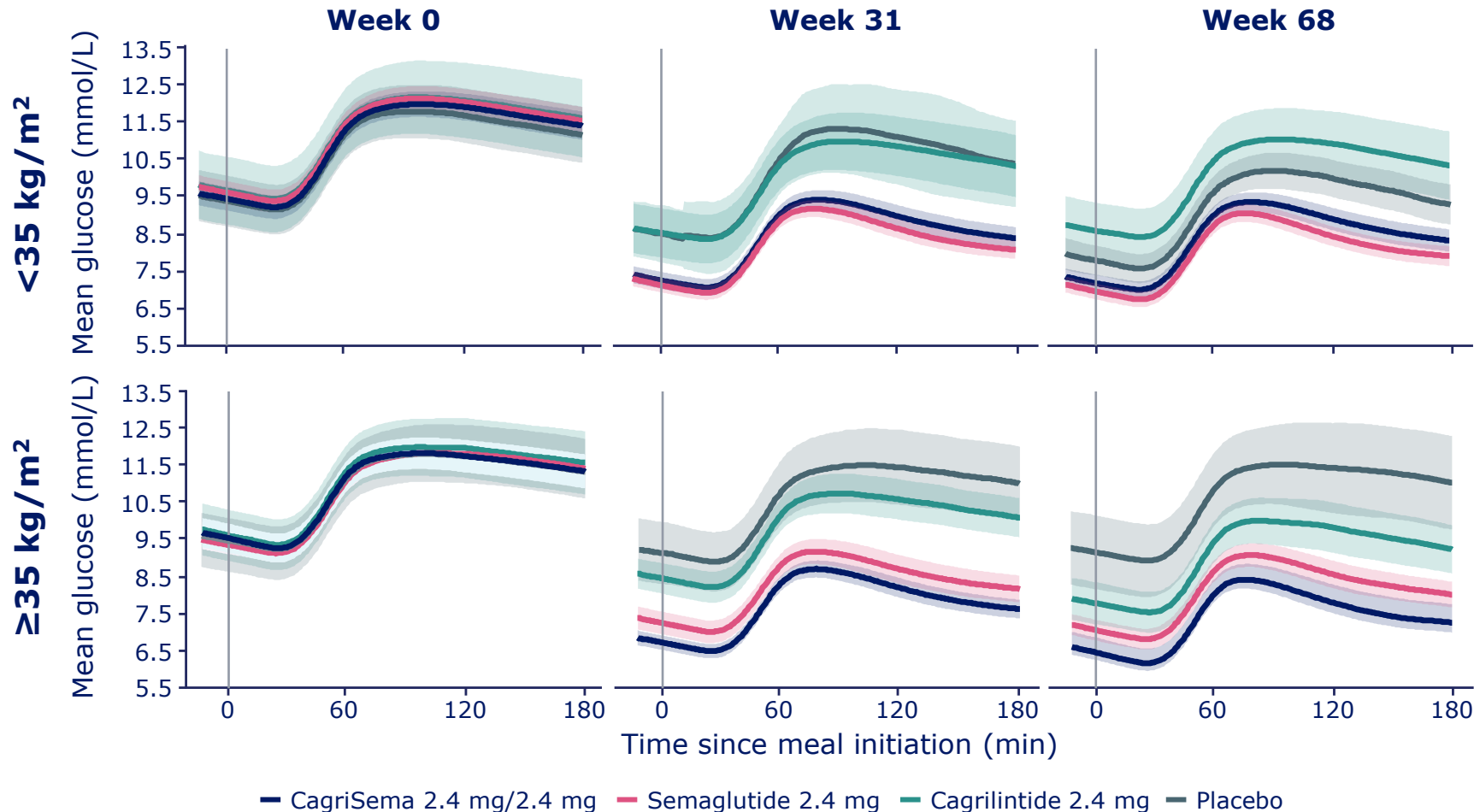
Time spent at various glucose ranges by baseline BMI



At week 68, treatment differences with CagriSema 2.4 mg/2.4 mg vs semaglutide 2.4 mg in TIR and TITR were significantly better for people with BMI ≥ 35 kg/m² than in those with BMI < 35 kg/m² (treatment-by-subgroup interaction $p=0.0135$ [TIR] and $p=0.006$ [TITR])

Data are observed values for the on-treatment without rescue period in the CGM group.
BMI, body mass index; CGM, continuous glucose monitoring; TIR, time in range; TITR, time in tight range.

Changes in PPG curves by baseline BMI



- In people with BMI $\geq 35 \text{ kg/m}^2$, all treatments improved PPG curves vs placebo at week 68
- The efficacy was consistent regardless of baseline BMI with semaglutide 2.4 mg, but efficacy was greater in people with BMI $\geq 35 \text{ kg/m}^2$ with CagriSema 2.4 mg/2.4 mg
- Time to normoglycaemia ($<7.8 \text{ mmol/L}$) improved with CagriSema 2.4 mg/2.4 mg and semaglutide 2.4 mg vs placebo

Conclusion: These data support CagriSema 2.4 mg/2.4 mg for improved glucose control, especially in people with BMI $\geq 35 \text{ kg/m}^2$

*Data are estimated means for the efficacy estimand. Shaded areas represent 95% confidence intervals.
BMI, body mass index; PPG, post-prandial glucose.*

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- This was a prespecified substudy to assess continuous glucose monitoring (CGM) parameters in a subgroup of participants from the REIMAGINE 2 study at three time points.

- CagriSema is a fixed-dose combination of cagrilintide and semaglutide.
- In REIMAGINE 2, CagriSema 2.4 mg/2.4 mg significantly reduced glycated haemoglobin (HbA_{1c}) and body weight versus its monocomponents in people with type 2 diabetes inadequately controlled on metformin ± sodium-glucose cotransporter-2 inhibitor, and overweight/obesity¹
- In a subgroup of participants, CGM parameters were collected.

- REIMAGINE 2 was a 68-week, randomised, double-blind, placebo- and active-controlled parallel group phase 3 study (Figure 1).¹
- People were randomised to once-weekly subcutaneous CagriSema 2.4 mg/2.4 mg, semaglutide 2.4 mg, cagrilintide 2.4 mg, CagriSema 1.0 mg/1.0 mg, semaglutide 1.0 mg or dose-matched placebo.
 - In this analysis, only data for participants who received CagriSema 2.4 mg/2.4 mg, semaglutide 2.4 mg, cagrilintide 2.4 mg and placebo have been reported.
- At screening, week 28 and 20 days before week 68 (approximately week 65), people in the CGM subgroup (*n*=1298) were provided with Dexcom G6[®] CGM devices for 20 days, with readouts at week 0 (baseline), week 31 and week 68.
- Time in range (TIR; 3.9–10.0 mmol/L) and time in tight range (TTR; 3.9–7.8 mmol/L) were confirmatory secondary endpoints assessed in the CGM subgroup.
- Post-prandial glucose (PPG) assessments, including area under the curve from 0 to 180 minutes ($AUC_{0-180\text{ min}}$) and time to normoglycaemia were post hoc analyses.
- Time to normoglycaemia used time from meal initiation to 180 minutes post-meal and was estimated with the Glucose Rate Increase Detector algorithm.²
- Estimated data are for the efficacy estimand.

The flowchart illustrates the study design. It begins with randomisation (R) in a 1:1:1:1 ratio, splitting participants into four groups: Cagrisema 2.4 mg/2.4 mg, Semaglutide 2.4 mg, Cagrisema 1.0 mg/1.0 mg, and Placebo 2.4 mg/2.4 mg. Each group receives its respective treatment for 816 weeks. After this period, participants are followed up for 7 weeks. The follow-up period is divided into three continuous glucose monitoring (CGM) periods: CGM period 1 (from -3 to 0 weeks), CGM period 2 (from 28 to 31 weeks), and CGM period 3 (from 65 to 68 weeks). The total duration of the study is 823 weeks.

A. Change in HbA_{1c}

Mean at baseline: 8.2%

Mean (change in HbA_{1c}, %) (p-value)

Treatment	Mean (change in HbA _{1c} , %)
CagTems 2.4 mg	-1.99
Semaglutide 2.4 mg	-1.74
CagTems 2.4 mg + Semaglutide 2.4 mg	-0.69
Placebo	-0.31

p=0.05

p<0.0001

p<0.0001

p<0.0001

B. Change in body weight

Mean at baseline: 102.4 kg

Mean (change in body weight) (kg)

Treatment	Mean (change in body weight) (kg)
CagTems 2.4 mg	-14.2
Semaglutide 2.4 mg	-10.0
CagTems 2.4 mg + Semaglutide 2.4 mg	-8.6
Placebo	-1.6

p<0.0001

p<0.0001

p<0.0001

p<0.0001

Legend: CagTems 2.4 mg (dark blue), Semaglutide 2.4 mg (pink), CagTems 2.4 mg + Semaglutide 2.4 mg (teal), Placebo (grey)

Data are estimated mean changes according to the efficacy estimand. p values are not adjusted for multiplicity. CGM, continuous glucose monitoring; HbA_{1c}, glycated haemoglobin.

Figure 1 Data: Mean percentage of observed time spent in TIR and TITR

Treatment	Time Point	TIR (%)			TITR (%)		
		<3.0	3.0-3.9	3.9-10.0	3.9-7.8	>10.0-13.9	>13.9
Cagrisema 2.4 mg/2.4 mg	Baseline	13.0	15.9	71.1	11.0	1.5	75.5
	Week 31	13.0	15.9	71.1	11.0	1.5	75.5
	Week 68	13.0	15.9	71.1	11.0	1.5	75.5
Semaglutide 2.4 mg	Baseline	14.4	11.6	74.0	11.2	1.3	77.5
	Week 31	14.4	11.6	74.0	11.2	1.3	77.5
	Week 68	14.4	11.6	74.0	11.2	1.3	77.5
Cagrilintide 2.4 mg	Baseline	17.6	15.9	66.5	13.4	2.4	70.9
	Week 31	17.6	15.9	66.5	13.4	2.4	70.9
	Week 68	17.6	15.9	66.5	13.4	2.4	70.9
Placebo	Baseline	13.2	7.3	79.5	10.2	2.5	78.0
	Week 31	13.2	7.3	79.5	10.2	2.5	78.0
	Week 68	13.2	7.3	79.5	10.2	2.5	78.0

Legend:

- <3.0 mmol/L (Red)
- 3.0-3.9 mmol/L (Pink)
- 3.9-10.0 mmol/L (TIR) (Green)
- 3.9-7.8 mmol/L (TITR) (Dark Green)
- >10.0-13.9 mmol/L (Light Green)
- >13.9 mmol/L (Yellow)

Data Source: Data are mean percentage of observed time spent in TIR and TITR for the on-treatment period. CGM, continuous glucose monitoring; TIR, time in range; TITR, time in tight range.

Capripima 2.4 mg/2.4 mg

Time point	<25 log ₁₀ IU/ml	≥25 log ₁₀ IU/ml
Week 0	12.8	13.9
Week 31	12.8	7.2
Week 68	11.8	6.8

Semaglutide 2.4 mg

Time point	<25 log ₁₀ IU/ml	≥25 log ₁₀ IU/ml
Week 0	15.4	12.4
Week 31	11.1	12.4
Week 68	10.7	12.1

Graprilinide 2.4 mg

Time point	<25 log ₁₀ IU/ml	≥25 log ₁₀ IU/ml
Week 0	18.9	15.6
Week 31	14.4	14.4
Week 68	14.4	13.1

Placebo

Time point	<25 log ₁₀ IU/ml	≥25 log ₁₀ IU/ml
Week 0	12.7	14.2
Week 31	25.2	14.2
Week 68	19.0	11.8

Legend:

- <25 log₁₀ IU/ml
- ≥25 log₁₀ IU/ml
- 3.9–10.9 nmol/L (TTR)
- 3.9–7.8 nmol/L (TTR)
- >10.9–13.9 nmol/L
- >13.9 nmol/L

Data are observed values for the on-treatment without rescue period in the CGM group.
IMU: body mass index; CGM, continuous glucose monitoring; TTR, time in range; TTR, time in tight range.

A. BMI <35 kg/m²

Week 0 Week 31 Week 68

Mean glucose (mmol/L)

Time since meal initiation (min)

Legend: CagriSema 2.4 mg/2.4 mg (black), Semaglutide 2.4 mg (red), CagriVidre 2.4 mg (green), Placebo (grey)

B. BMI ≥35 kg/m²

Week 0 Week 31 Week 68

Mean glucose (mmol/L)

Time since meal initiation (min)

Legend: CagriSema 2.4 mg/2.4 mg (black), Semaglutide 2.4 mg (red), CagriVidre 2.4 mg (green), Placebo (grey)

Data are estimated means for the efficacy endpoint. Shaded areas represent 95% confidence intervals. BMI, body mass index; PPG, post-prandial glucose.

- Overall, 288 people in the CGM subgroup received CagriSema 2.4 mg/2.4 mg, 290 received semaglutide 2.4 mg, 73 received cagrilintide 2.4 mg and 71 received placebo.
- Baseline characteristics were similar between groups; most people were male (57.9%), with a mean age of 58.6 years, body weight of 102.4 kg, body mass index (BMI) of 35.2 kg/m² and HbA_{1c} of 8.2%.

Mean changes in HbA_{1c} and body weight in the CGM subgroup

- Mean change in HbA_{1c} and relative change in body weight from baseline to week 68 were significantly greater with CagriSema 2.4 mg/2.4 mg versus its monocomponents and placebo in the CGM subgroup (Figure 2).

- Improvements in TIR and TITR across treatment groups were evident by week 31 and continued through week 68 (Figure 3).
- At week 68, treatment differences with CagriSema 2.4 mg/2.4 mg versus semaglutide 2.4 mg in TIR and TITR were greater for people with BMI ≥ 35 kg/m² than in those with BMI < 35 kg/m² (treatment-by-subgroup interaction $p=0.0135$ [TIR] and $p=0.006$ [TITR]; Figure 4).

- PPG curves across treatment groups were similar at baseline, with improvements seen at week 31 for CagriSema 2.4 mg/2.4 mg and semaglutide 2.4 mg versus placebo.
- In people with BMI ≥ 35 kg/m² at baseline, all treatments improved PGI curves at week 68 versus placebo, with greater efficacy seen with CagriSema 2.4 mg/2.4 mg than semaglutide 2.4 mg (Figure 5).
- Time to normoglycaemia (glucose <7.8 mmol/L) improved from baseline with CagriSema 2.4 mg/2.4 mg and semaglutide 2.4 mg versus placebo (estimated least-square mean [95% confidence interval]: -32.2 min [-5.50, -29.5] and -30.5 min [-33.3, -27.8] vs -0.1 min [-7.2, 7.0], respectively).
- The effect was consistent regardless of baseline BMI with semaglutide (-30.4 vs -30.3 min in participants with BMI ≥ 35 kg/m² vs BMI <35 kg/m²), but was greater in people with higher baseline BMI with CagriSema 2.4 mg/2.4 mg (-40.2 vs -26.2 min in participants with BMI ≥ 35 kg/m² vs BMI <35 kg/m², respectively).

- CagriSema 2.4 mg/2.4 mg and semaglutide 2.4 mg led to clinically relevant improvements in TIR, T1TR, PPG curves and time to normoglycaemia.
- Improvements with CagriSema 2.4 mg/2.4 mg were greatest in people with baseline BMI ≥ 35 kg/m².
- Semaglutide 2.4 mg efficacy was consistent regardless of baseline BMI.
- These data support this combination therapy for improved glucose control, especially in people with BMI ≥ 35 kg/m².

[illegible]

Reference

(1) Kase, B. et al. *Lancet Diabetes Endocrinol* 2020;14(12):67.

(2) Hannon, B.B. et al. *J Diabetes Sci Technol* 2016;8(20):393-395.