A Novel Approach to Weight Loss in Women Over 50 Years: Insights from the RESET Study with a Shape-Shifting Hydrogel Capsule

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BACKGROUND

Approximately 50%–70% of women experience measurable weight gain during the menopausal transition, averaging ≈1.5 kg per year in perimenopause. These changes are closely linked to the decline in estradiol, which drives increased fat mass and visceral adiposity and raises cardiometabolic risk.

Menopause is also a period of vulnerability in appetite regulation and satiety signalling. Hormone therapy (HT) can partially mitigate these changes, but it is not suitable, accepted or preferred by all women — making non-hormonal, satiety-enhancing interventions particularly well suited to this population.

THE EPITOMEE CAPSULE

The Epitomee capsule is an FDA-cleared, CE-marked, drug-free oral device for weight management in adults with overweight or obesity (BMI 25–40 kg/m²). Taken twice daily with two cups of water before lunch and dinner, it expands in the stomach into a semi-rigid, pH-sensitive triangular gel structure (97% water, 3% polymers) that resists peristaltic waves, activates sensory mechanoreceptors and promotes **early satiety through an entirely mechanical, non-systemic mechanism**. Within 30 min of reaching the intestine it disintegrates and is excreted through the GI tract.



Figure 1. Epitomee oral hydrogel capsule, and after shape-shifting in the stomach.

STUDY AIM

To evaluate the efficacy and safety of the Epitomee capsule versus placebo, in conjunction with lifestyle intervention, in women aged ≥50 years — a largely postmenopausal population not receiving HT — enrolled in the RESET study.

METHODS

- **Post-hoc sub-analysis** of the double-blind, placebo-controlled RESET study (NCT04222322) in **104 women aged ≥50 years**.
- Randomized 1:1 to Epitomee (n = 52) or matching placebo (n = 52) for 24 weeks, both combined with the same standardized lifestyle intervention (14 counselling sessions; 1,200–1,800 kcal/day; ≥180 min/week of activity by week 24).
- **Menopausal status & HT:** 90.4% postmenopausal and 9.6% premenopausal in both groups; only 3 participants received HT (1 Epitomee, 2 placebo).
- Capsules taken twice daily with two cups of water (480 mL) before lunch and dinner.
- **Primary endpoint:** percent change in body weight from baseline to week 24. **Secondary:** responder rates (≥5%, ≥10%, ≥15%), BMI category change, waist circumference and glycemic status; safety coded per MedDRA.
- Mixed-model repeated measures adjusted for baseline weight; logistic regression for responder analyses; significance set at P < 0.05.

KEY FINDINGS

−7.6% vs −4.4%	mean weight loss at week 24 (P = 0.0287)
63% vs 42%	achieved ≥5% weight loss (P = 0.0463)
29% vs 9%	achieved ≥10% weight loss (P = 0.0169)
56% vs 21%	improved BMI category (P = 0.0007)
0	device-related serious adverse events

BASELINE CHARACTERISTICS

	Epitomee (n = 52)	Placebo (n = 52)
Age at screening, mean [SD], y	59.2 [6.4]	57.6 [6.1]
BMI, kg/m², mean [SD]	33.6 [3.1]	33.4 [3.3]
Waist, cm, mean [SD]	105.3 [9.8]	104.1 [8.6]
High risk of chronic disease, n [%]	49 [94.2]	50 [96.2]
Race or ethnicity, n [%]		
Caucasian	36 [69.2]	32 [61.5]
Black or African American	11 [21.2]	18 [34.6]
Other	5 [9.6]	2 [3.8]
Childbearing status, n [%]		
Premenopausal	5 [9.6]	5 [9.6]
Postmenopausal	47 [90.4]	47 [90.4]
Randomization BMI class, n [%]		
Overweight	4 [7.7]	10 [19.2]
Class I obesity	29 [55.8]	24 [46.2]
Class II obesity	18 [34.6]	18 [34.6]
Class III obesity	1 [1.9]	0 [0.0]
FPG, mg/dL, mean [SD]	91.9 [8.5]	92.0 [9.5]
HbA1c, %, mean [SD]	5.7 [0.3]	5.6 [0.3]
Glycemic status, n [%]		
Normoglycemic	21 [40.4]	27 [51.9]
Prediabetic	29 [55.8]	25 [48.1]
Diabetes	1 [1.9]	0 [0.0]

Table 1. Demographic and baseline characteristics of women aged ≥50 years. Groups were comparable at baseline. Dropout was 7.7% (Epitomee) vs 17.3% (placebo), P = NS.

RESULTS · WEIGHT LOSS

Least-squares mean change in body weight from baseline to week 24 was **−7.6% with Epitomee versus −4.4% with placebo (P = 0.0287)**. Separation from placebo emerged early, and weight loss was progressive and continuous throughout the 24-week treatment period.

−7.6%	−4.4%	P = 0.0287
Epitomee, week 24	Placebo, week 24	LS mean difference

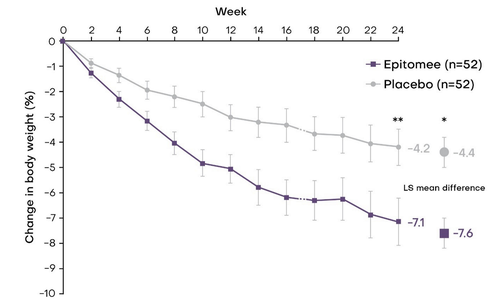


Figure 2. Mean percent change in body weight from baseline to week 24 in female participants ≥50 years (n = 104).

RESPONDER ANALYSIS

Significantly more Epitomee-treated women reached clinically meaningful weight-loss thresholds: **≥5% in 63% vs 42% (P = 0.0463)** and **≥10% in 29% vs 9% (P = 0.0169)**. ≥15% weight loss was numerically higher with Epitomee (13% vs 5%, P = 0.1903).

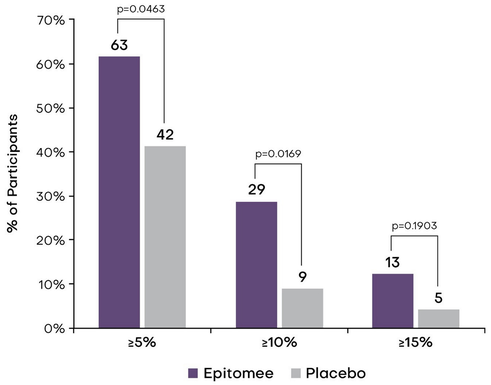


Figure 3. Proportion of female participants ≥50 years with a reduction in body weight from baseline to week 24 of ≥5%, ≥10% and ≥15%.

EARLY RESPONDERS

Early response (ER) was defined as ≥2% weight loss at week 8. Among women >50 years classified as early responders, mean weight reduction at week 24 was:

9.9% ± 5.7%	6.2% ± 4.4%	P = 0.0074
Epitomee	Placebo	ER comparison

METABOLIC & GLYCEMIC TRENDS

- **Waist circumference:** −6.2 ± 2.8 cm with Epitomee vs −4.8 ± 2.5 cm with placebo at week 24 (−4.4 vs −2.3 cm at week 12).
- **Glycemic status:** 35% of Epitomee-treated participants shifted from prediabetes to normoglycemia vs 29% with placebo; fewer shifted from normoglycemia to prediabetes (22% vs 29%). These differences did not reach statistical significance.

BMI CATEGORY IMPROVEMENT

56% of Epitomee participants improved their BMI category by at least one tier, versus 21% with placebo (P = 0.0007).

With Epitomee, Class III obesity fell from 2.1% to 0% and Class II from 35.4% to 16.7%, while the overweight category rose from 8.3% to 25.0% and normal weight from 0% to 14.6%. The placebo group showed limited overall change, with Class I obesity increasing (44.2% → 51.2%).

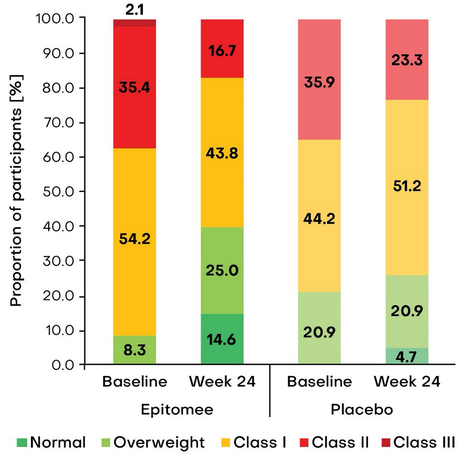


Figure 4. Change in BMI category among female participants aged ≥50 years at baseline and week 24. Normal 18.5–24.9; overweight 25.0–29.9; class I 30.0–34.9; class II 35.0–39.9; class III ≥40 kg/m².

SAFETY

Overall adverse-event (AE) incidence was similar between groups — **86.5% with Epitomee vs 90.4% with placebo (P = NS)** — with mild events most common. GI-related AEs were numerically **lower** with Epitomee (38.5% vs 50.0%, P = NS). **No serious AEs and no device-related SAEs occurred.**

The most common AEs with Epitomee were constipation (14%), nasopharyngitis (14%), COVID-19 (12%), arthralgia (8%), abdominal pain (8%) and upper respiratory tract infection (8%).

	Epitomee (n = 52)		Placebo (n = 52)	
	Events	Subjects (%)	Events	Subjects (%)
Adverse events (AEs)	122	45 (87)	156	47 (90)
Severe AEs	4	4 (8)	8	4 (8)
Serious AEs	0	0 (0)	0	0 (0)
GI-related AEs	30	20 (39)	45	26 (50)

Table 2. Total, severe, serious and GI-related adverse events in women aged ≥50 years.

ADVERSE EVENTS

A

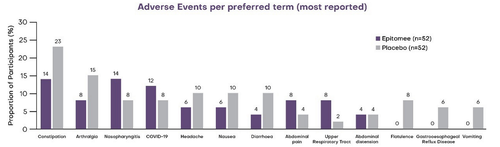


Figure 6A. Adverse events per preferred term (most reported).

B

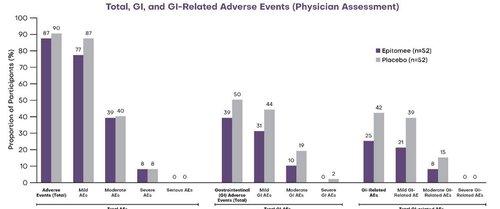


Figure 6B. Total, GI and GI-related adverse events (physician assessment).

CONCLUSIONS

- **The Epitomee capsule is an effective, drug-free oral device** promoting significant weight loss and BMI category improvement in women over 50.
- Clinical trends indicate improvements in metabolic health, including waist circumference reduction and shifts toward normoglycemia.
- **Epitomee is safe and well tolerated**, with a non-systemic safety profile comparable to placebo and no device-related serious adverse events.
- Epitomee is a promising non-pharmaceutical intervention for weight management in the menopausal population.
- **Limitations:** small sample size (n = 104) and short duration (24 weeks); larger and longer studies are needed.

FUNDING & DISCLOSURES

The study was funded by Epitomee Medical Ltd. Y.K. is an employee of Epitomee Medical and holds stock or stock options; L.C.A. is a past employee of Epitomee with no conflict of interest. G.S. reports advisory fees from Eli Lilly, Novo Nordisk, Rhythm, Quest Diagnostics and Epitomee Medical, research grant support from Novo Nordisk, and Speakers' Bureau participation for Novo Nordisk. M.K. reports consultancy fees from Exelixis, Uberlube, Reckitt Benckiser and the California Medical Board, and consults for Epitomee Medical (no fees to date). A.G. has received consultancy fees from Epitomee Medical, Eli Lilly, Novo Nordisk, Currax and Boehringer Ingelheim. B.D. consults for Epitomee Medical (no fees to date). D.D. has received speaker and advisory board fees, research grants and travel support from Boehringer Ingelheim, Eli Lilly, Novo Nordisk, AstraZeneca and Roach.

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weight management capsule

AE, adverse event; BMI, body mass index; ER, early responder; FPG, fasting plasma glucose; GI, gastrointestinal; HT, hormone therapy; LS, least squares; NS, not significant; SAE, serious adverse event; SD, standard deviation.