

Effect of CagriSema on bone biomarkers in participants with inadequately controlled type 2 diabetes: REIMAGINE 2

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Aim

- This exploratory analysis investigated the effects of CagriSema on bone turnover in people with inadequately controlled type 2 diabetes (T2D) and overweight or obesity.

Introduction

- T2D is associated with impaired bone cell function and suppressed bone turnover, including lower C-terminal cross-linked telopeptide of type 1 collagen (CTX-1) and procollagen-1 N-terminal propeptide (P1NP), and advanced glycation end product-mediated collagen brittleness, which may increase fracture risk despite preserved bone mineral density.^{1,2}
- Semaglutide may reduce fracture risk versus some weight-loss mechanisms, while cagrilintide may support glycaemic control, healthy weight loss and bone mass preservation through amylin and calcitonin receptor activation.¹⁻⁹
- REIMAGINE 2 assessed CagriSema, a fixed-dose cagrilintide and semaglutide combination, versus its monocomponents or placebo in participants with inadequately controlled T2D and overweight or obesity.¹⁰

Methods

- REIMAGINE 2 was a 68-week, randomised, double-blind, placebo- and active-controlled, parallel group, phase 3a study (**Figure 1**).¹⁰
- Eligible participants were aged ≥ 18 years with T2D uncontrolled on stable metformin $\pm$ sodium-glucose cotransporter-2 inhibitor with glycated haemoglobin (HbA_{1c}) 7.0–10.5% and body mass index (BMI) ≥ 25 kg/m².
- Fasting blood samples were obtained at baseline and weeks 8, 20 and 68 for the measurement of CTX-1 and P1NP.
- Estimated data are for the efficacy estimand.
- Analysis of bone biomarkers focused on CagriSema 2.4 mg/2.4 mg and 1.0 mg/1.0 mg and semaglutide 2.4 mg, as these study arms had the greatest weight loss.

Figure 1. REIMAGINE 2 study design

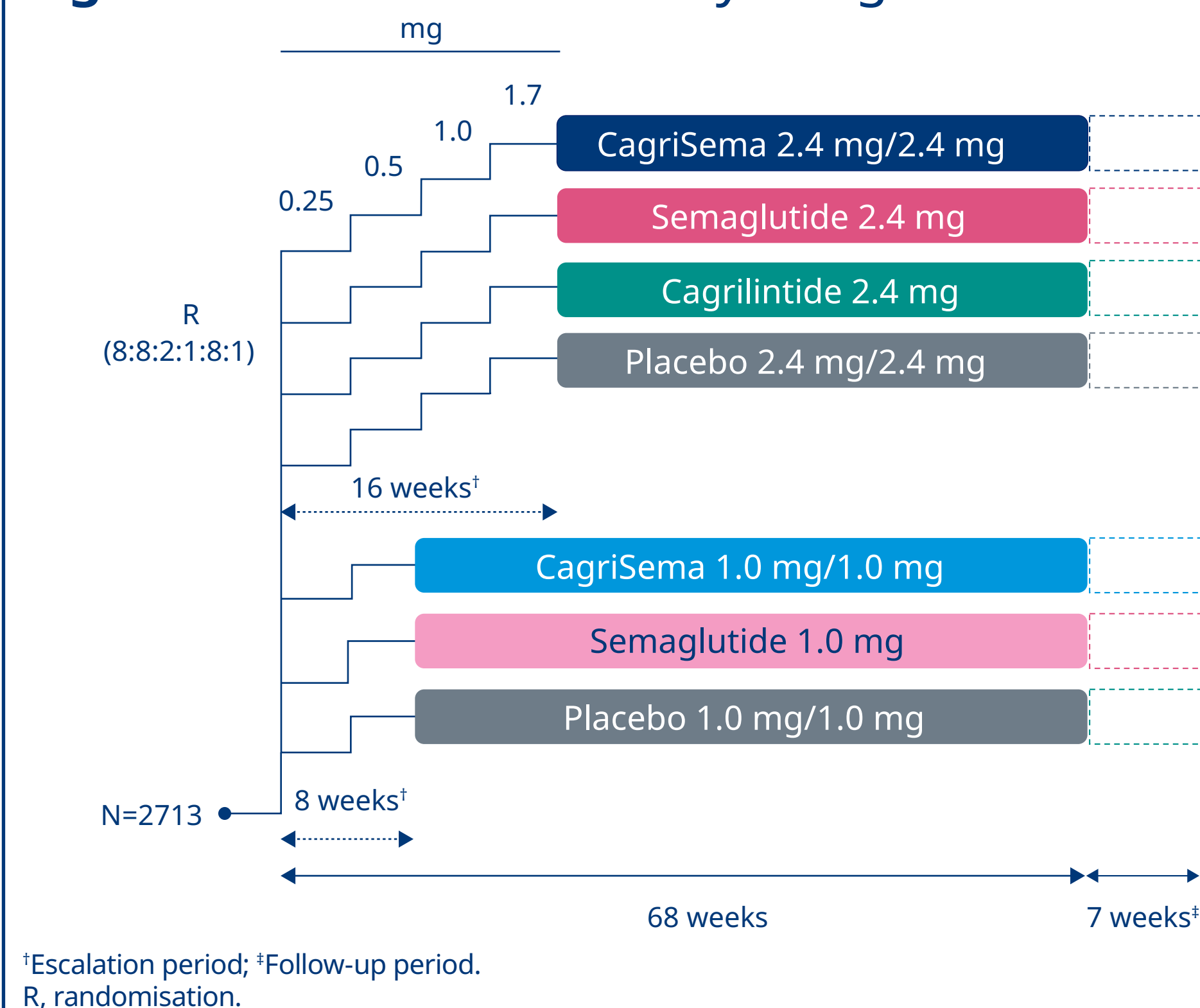


Figure 2. CagriSema led to superior body weight reductions versus semaglutide and cagrilintide in REIMAGINE 2

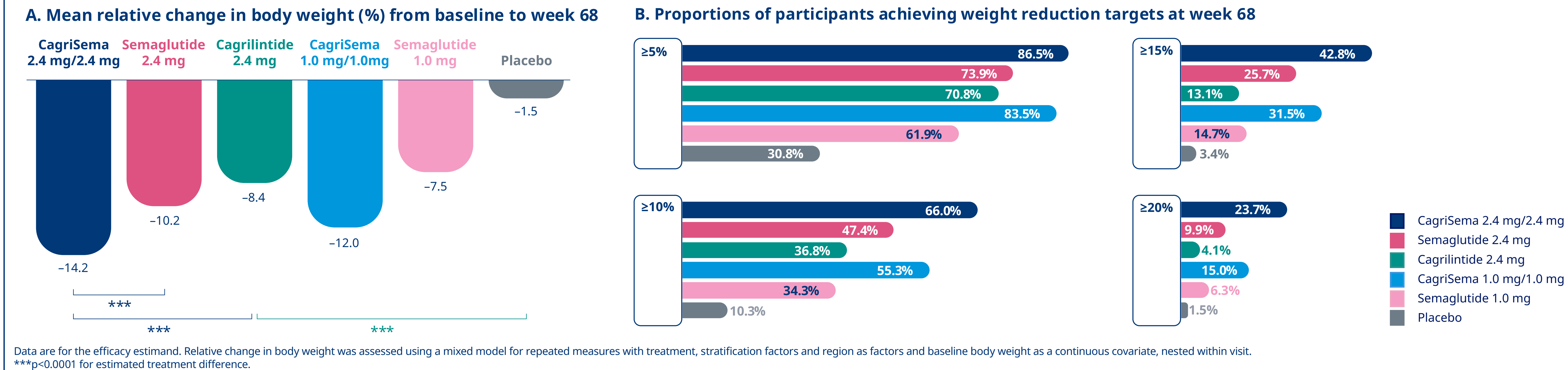
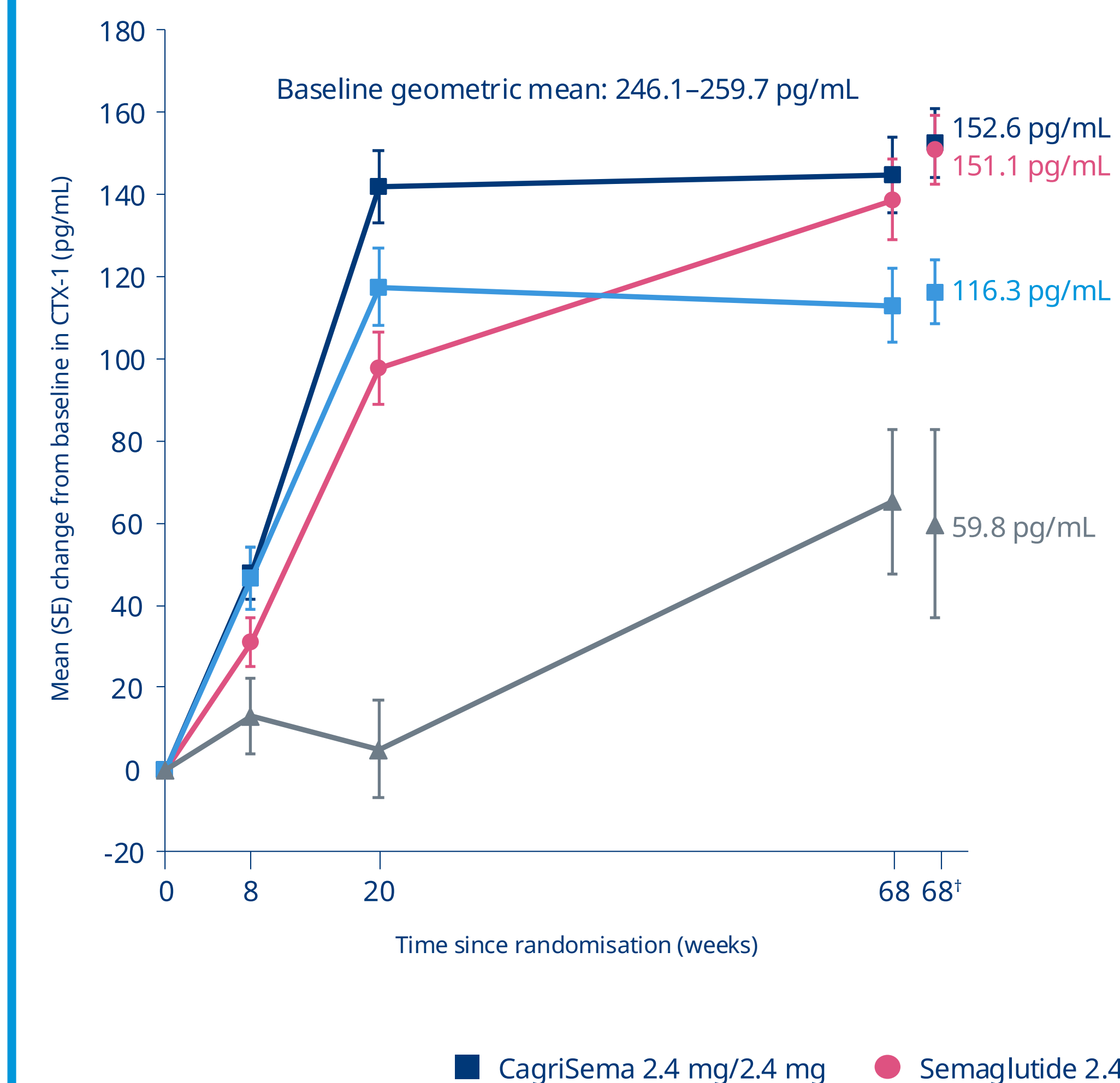


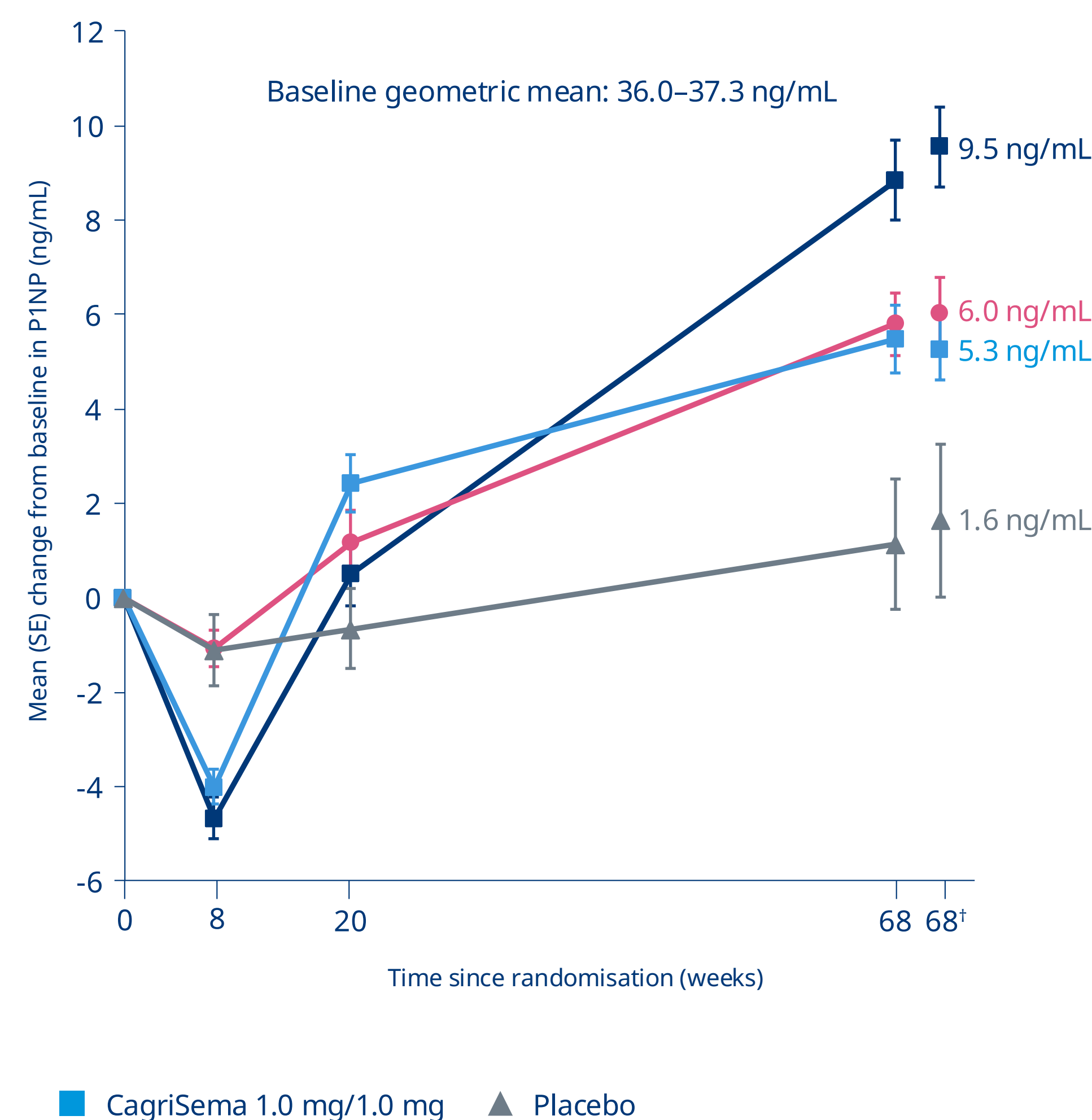
Figure 3. CagriSema was associated with changes in CTX-1 and P1NP from baseline to week 68 that are consistent with reactivation of bone remodelling

Key Result

A. Mean change from baseline in CTX-1 (bone resorption)



B. Mean change from baseline in P1NP (bone formation)



*Estimated mean change at week 68 for the efficacy estimand; analyses used a mixed model for repeated measures with treatment, stratification factors and region as factors and baseline factor as a continuous covariate, nested within visit. CTX-1, C-terminal cross-linked telopeptide of type 1 collagen; P1NP, procollagen-1 N-terminal propeptide; SE, standard error.

Results

- Baseline characteristics were similar between groups; overall, mean (standard deviation) age was 57.1 (10.5) years, BMI was 35.1 (6.8) kg/m², body weight was 100.9 (22.8) kg and 42.9% of participants were female.
- In REIMAGINE 2, HbA_{1c} reductions from baseline to week 68 were greater with CagriSema 2.4 mg/2.4 mg (-1.91%-points) and CagriSema 1.0 mg/1.0 mg (-1.82%-points) than with semaglutide 2.4 mg (-1.75%-points), semaglutide 1.0 mg (-1.54%-points), cagrilintide 2.4 mg (-0.80%-points), or placebo (+0.09%-points), using the efficacy estimand.¹⁰
- CagriSema also produced greater reductions in body weight versus its monocomponents (**Figure 2**).¹⁰
- CagriSema was associated with changes in CTX-1 and P1NP that are consistent with reactivation of bone remodelling (**Figure 3**).
- Mean CTX-1 levels increased to week 20 in all active treatment arms (**Figure 3A**), after which they stabilised in the CagriSema 2.4 mg/2.4 mg and 1.0 mg/1.0 mg arms between week 20 and week 68, whereas mean P1NP levels continued to increase from week 20 to week 68 (**Figure 3B**).

Conclusion

- In the context of the significant weight loss associated with CagriSema, CTX-1 levels increased initially and subsequently plateaued after week 20, indicating stabilisation of bone resorption through week 68.
- In parallel, P1NP continued to increase from week 20 to 68, suggesting ongoing bone formation activity following the initial remodelling response.
- The stabilisation of CTX-1, coupled with the increase in P1NP from week 20 to 68, provides preliminary reassurance regarding bone changes with CagriSema in T2D, pointing at a controlled bone turnover reactivation that may lead to beneficial effects on bone.

References

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