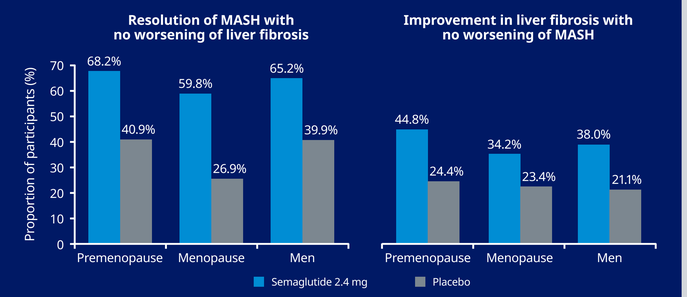
Semaglutide provides liver health-related benefits in menopausal women living with MASH: A *post hoc* analysis of the ESSENCE trial part 1

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In menopausal women with MASH, semaglutide 2.4 mg resulted in higher histologic response rates versus placebo, broadly comparable to premenopausal women and men



Aim

- Menopausal women with metabolic dysfunction-associated steatohepatitis (MASH) have an increased risk of advanced liver fibrosis and faster disease progression versus premenopausal women and men of a similar age.[1–3]
- This *post hoc* analysis of the ESSENCE trial assessed the effect of semaglutide 2.4 mg on liver histology and non-invasive tests (NITs) by menopause status.

Method

- Analyses were performed in menopausal and premenopausal women, classified by investigator-assessed child-bearing potential based on reproductive status and medical history, and in men.
- Proportions of participants achieving resolution of MASH with no worsening of liver fibrosis and improvement in liver fibrosis with no worsening of MASH at week 72 were evaluated.
- Changes from baseline to week 72 in NITs were also assessed, including alanine aminotransferase, liver stiffness by vibration-controlled transient elastography, Enhanced Liver Fibrosis and FibroScan-AST.

Key results

- Participant baseline characteristics are presented in **Table 1**.
- Semaglutide showed numerically higher histologic responses versus placebo across subgroups (**banner figure**):
  - Estimated difference in responder proportions for resolution of MASH with no worsening of liver fibrosis: premenopause 27.3% (95% CI 2.3, 52.3; p=0.0325); menopause 32.9% (95% confidence interval [CI] 22.0, 43.7; p<0.0001); men 25.3% (95% CI 13.9, 36.7; p<0.0001).
  - Estimated difference in responder proportions for improvement in liver fibrosis with no worsening of MASH: premenopause 20.3% (95% CI –2.4, 43.0; p=0.0793); menopause 10.8% (95% CI 0.5, 21.1; p=0.0406); men 16.9% (95% CI 6.7, 27.1; p=0.0012).
- For NITs, semaglutide showed consistent and comparable improvements versus placebo across premenopause, menopause and men subgroups, with most statistically significant (**Figure 1**).

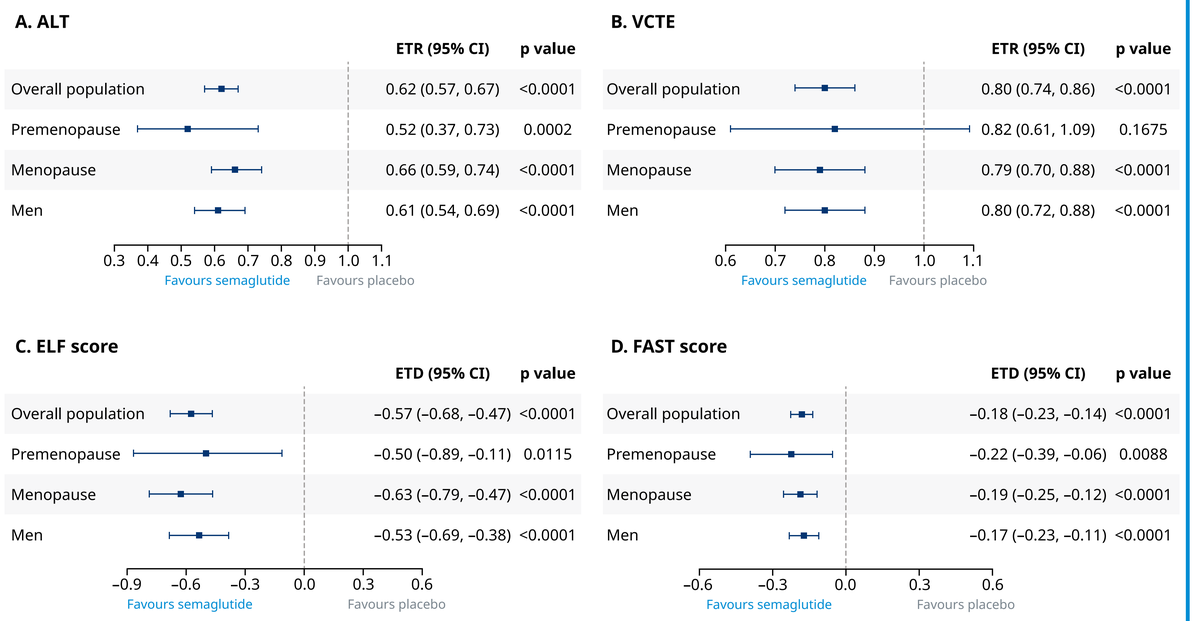
Table 1. Baseline characteristics

Baseline characteristic	Premenopause (n=82)	Menopause (n=375)	Men (n=343)
Age, years	42.2 ± 8.1	61.0 ± 8.5	53.9 ± 11.9
Body weight, kg	98.9 ± 22.8	85.7 ± 19.9	106.8 ± 24.7
Waist circumference, cm	113.6 ± 15.9	108.4 ± 14.5	116.2 ± 16.1
BMI, kg/m^2	37.7 ± 8.1	33.5 ± 6.9	34.9 ± 7.1
<25, n (%)	3 (3.7)	38 (10.1)	12 (3.5)
≥25–<30, n (%)	11 (13.4)	86 (22.9)	67 (19.5)
≥30–<35, n (%)	19 (23.2)	118 (31.5)	115 (33.5)
≥35, n (%)	49 (59.8)	133 (35.5)	148 (43.1)
Fibrosis stage 2, n (%)	32 (39.0)	101 (26.9)	117 (34.1)
Fibrosis stage 3, n (%)	50 (61.0)	274 (73.1)	226 (65.9)
T2D, n (%)	38 (46.3)	232 (61.9)	177 (51.6)

Data are mean ± SD, unless otherwise stated.
BMI, body mass index; SD, standard deviation; T2D, type 2 diabetes.

Figure 1. Changes from baseline to week 72 in NITs

Key results



Data were analysed by analysis of covariance with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline parameters as covariates. Missing data were imputed from observed data in the placebo group using the same analysis of covariance model but without treatment as a factor.
ALT, alanine aminotransferase; CI, confidence interval; ELF, Enhanced Liver Fibrosis; ETD, estimated treatment difference; ETR, estimated treatment ratio; FAST, FibroScan-AST; NITs, non-invasive tests; VCTE, vibration-controlled transient elastography.

Conclusion

- Semaglutide improved liver histology and NITs in participants with MASH across premenopause, menopause and men subgroups.
- Menopause does not reduce the likelihood of achieving liver health improvements with semaglutide.

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