Theramex Initiated and Sponsored Non-Interventional Study

Study Summary

Title
Major Adverse Cardiovascular Event Risk in Menopausal Women treated With Oral Estradiol/Micronized Progesterone Versus Conjugated Estrogens/Medroxyprogesterone: US Data Claims Analysis

Study Sponsor
Theramex Ltd, 5th Floor, 50 Broadway, London, SW1H 0BL

Status
Completed

Objectives
To compare the risk of major adverse cardiovascular events (MACE) between two combined oral therapies available to women in the US: estradiol/micronized progesterone (E2/P4) and conjugated equine estrogens/medroxyprogesterone acetate (CEE/MPA) using the real-world data

Study Type
Observational, retrospective longitudinal, non-interventional study of the Symphony US claims database (04/2019 to 06/2021)

Study Population
- E2/P4 cohort included 6,520 menopausal women [the mean (± SD) age at index date was 55.8 ± 6.5 years]
- CEE/MPA cohort included 29,426 menopausal women [the mean (± SD) age at index date was 56.1 ± 6.3 years]
- Total: 35,673 women

Study Timelines
March 2023 - March 2024

Methodology
Women were eligible if:

- Absence of MACE events (hospitalisation with MI, stroke, or heart failure diagnosis) before or on the study entry (first prescription fill)
- ≥1 medical and ≥1 pharmacy claim during the baseline period and demonstrated continuous medical and pharmacy activity for at least six months following initiation of E2/P4 or CEE/MPA

Outcomes were measured from the index date to the earliest of the day before switch to the comparator treatment, the data cut-off date in June 2021, or the end of clinical activity (observation period; ≥6 months by design).

MACE Measures (events included hospitalisation) for:

- Acute myocardial infarction
- Ischemic or haemorrhagic stroke
- Heart failure

- Revascularisation procedures indicative of MI observed during or the day before a hospitalization

Statistical analysis
The risk of major cardiovascular events was compared between women taking E2/P4 and those taking CEE/MPA, with statistical methods used to adjust for baseline differences between groups.

Study Location
US

Ethics Approval
N/A

Summary of Results
- In the IPT-weighted analyses, MACE events rates were 23.5 and 85.4 per 10,000 women-years among women receiving E2/P4 and CEE/MPA, respectively (IPT-weighted incidence rate ratio [IRR] 0.28, 95% CI 0.17 - 0.45
- In analyses by event type of MACE, all three MACE event types were associated with lower relative risks for E2/P4 as compared to CEE/MPA (IPT-weighted IRRs 0.24, 0.22, and 0.32 for heart failure, acute MI, and stroke, respectively; all $p< 0.001$)

Conclusions
In IPT time to event analyses, the probability of experiencing a MACE event was lower for women receiving E2/P4 than for those receiving CEE/MPA (IPT-weighted hazard ratio [HR] 0.28, 95% CI 0.17-0.46)

Limitations
- Symphony database, while extensive, may miss some medical visits/dispensations of drug prescriptions and may also contain occasional coding errors
- Because the Symphony database does not include information on date of death or cause of death, we were unable to account for death either as an event (cardiovascular death) or as a competing risk (other death)
- By using the Symphony database (open claims), the study was limited to women from the USA who had regular clinical activity (i.e. pharmacy and medical claims) during the study period.

Reference
The study results published in a peer-reviewed journal: Climacteric (2025) Aug 7:1-11 DOI: 10.1080/136137.2025985