Study Summary

Title
Oral estradiol/micronised progesterone may be associated with lower risk of venous thromboembolism compared with conjugated equine estrogens/ medroxyprogesterone acetate in real-world practice.

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

Status
Completed.

Objectives
Primary objectives:
- To describe and compare demographic and clinical characteristics of menopausal women.

Exploratory objective:
- To compare risk of venous thromboembolism (VTE) between women treated with the combined oral therapies: estradiol/micronised progesterone (E2/P4) or 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 6,526 menopausal women [the mean (± SD) age at index date was 54.9 ± 11.2 years].
- CEE/MPA cohort included 29,535 menopausal women [the mean (± SD) age at index date was 55.9 ± 6.0 years].
- Total: 36,061 women.

Methodology
Women were required to have:
- No VTE diagnosis prior to the index date (initiation of the study).
- ≥ 1 medical and ≥ 1 pharmacy claim during the baseline period (prior to initiation of the study).
- 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).

Data Analysis
The risk of venous thromboembolism (VTE) events was compared between women taking E2/P4 and those taking CEE/MPA, with statistical methods used to adjust for baseline differences between groups, Inverse Probability of Treatment Weighting (IPT-weighting).

Study Location
United States.

Ethics approval
N/A.

Summary of Results
- Baseline patients' demographics and clinical characteristic (before to IPT- weighting) women receiving oral E2/P4 were younger than those receiving oral CEE/MPA (mean age: 54 vs 56 years), had less cardiovascular disease (34 % vs 44 %), less hypercholesterolemia (24 % vs 31 %).
- Exploratory objectives results:
    i. VTE incidence (post IPT weighting).
        1. For women receiving oral E2/P4 incidence rate: 37 per 10 000 women's years.
        2. For women receiving oral CEE/MPA incidence rate: 53 per 10 000 women's years.
        3. IPT-weighted incidence rate ratio [IRR] 0.70, 95 % CI 0.53–0.92).

Conclusions

After controlling for many potential confounders, the current study found that women treated with oral E2/P4 had a significantly lower risk of VTE than women treated with oral CEE/MPA. Since VTEs are relatively rare events, further studies with different data sources are needed to confirm the findings of these exploratory analyses.

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.
- Further studies with different data sources are needed to confirm the findings of the current exploratory analyses.

Reference:

The study results are published in a peer-reviewed journal: Panay N, Nappi RE, Stute P, Palacios S, Paszkowski T, Kagan R, Archer DF, Héroux J, Boolell M. Oral estradiol/micronised progesterone may be associated with lower risk of venous thromboembolism compared with conjugated equine estrogens/medroxyprogesterone acetate in real-world practice. *Maturitas Jun;172:23-31 (2023). doi:10.1016/j.maturitas.2023.04.004.*