Case study

Evaluating the safety of hormone therapies for menopausal symptoms

How we compared conjugated estrogens/bazedoxifene with estrogen/progestin to provide clearer safety insights for women

carelon

Challenge

Safety concerns of hormone therapy for menopausal symptoms

Hormone therapy is an effective treatment for menopausal symptoms but estrogen can increase risk of endometrial cancer. This risk can be countered by progestin, but the addition of progestin in turn raises breast cancer risk. Selective estrogen receptor modulators (SERMs) such as bazedoxifene (BZA) offer an alternative to progestin in combined hormonal therapy for menopausal transition, but the risk:benefit is uncertain.

Objective

Assess the risk of endometrial cancer, endometrial hyperplasia, and breast cancer among women using conjugated estrogens/bazedoxifene (CE/BZA) compared with those using estrogen/progestin combination hormone therapy (EP).

Solution

A real world multi-database study using US healthcare databases

As the Scientific Coordinating Center, we conducted a European Medicines Agency-required post-authorization safety study using five U.S. healthcare claims databases encompassing over 92 million women from 2014 to 2019. CE/BZA and EP users were matched using propensity scores to ensure comparability. Incidence of endometrial safety outcomes was determined using validated claims-based algorithms. Rate ratios (RR) and differences were pooled across databases using random-effects models. The study leveraged extensive data sources and rigorous statistical methods to produce reliable results.

Data sources

- Aetna's Sentinel Common Data Model (CVS Health Clinical Trial Services)
- Carelon Research's Integrated Research Database (HIRD)
- MarketScan Commercial Claims and Encounters and Medicare Supplemental Databases
- MarketScan Medicaid Database
- Optum Research Database (ORD)

Statistical analysis

Incidence rates and rate ratios were calculated, with pooled estimates from random-effects models. Sensitivity analyses accounted for potential latency between exposure and risk periods.

Study population

Female health plan enrollees with at least 12 months of continuous enrollment before their first CE/BZA or EP prescription.

Results

Slightly higher risk of endometrial cancer and hyperplasia, lower risk of breast cancer

The study population included 10,596 CE/BZA and 33,818 PS-matched EP new users.

Endometrial cancer and hyperplasia

- Slightly higher rates among CE/BZA users (1.6 and 0.4 additional cases per 10,000 person-years), though precision was limited due to the small number of cases
- Endometrial cancer: RR 1.50 (95% CI, 0.79-2.88)
- Endometrial hyperplasia: RR 1.69 (95% CI, 0.51-5.61)

Breast cancer

- Lower incidence in CE/BZA users (9.1 fewer cases per 10,000 person-years; RR 0.79; 95% CI, 0.58-1.05)

Compared to EP users, CE/BZA users had a slightly higher risk of endometrial cancer and hyperplasia and a lower risk of breast cancer.

Impact

Informing clinicians and patients for safer hormone therapy choices

The findings indicate that CE/BZA may offer a safer alternative to EP for hormone therapy, particularly in reducing the risk of breast cancer. This information can aid clinicians and patients in making informed decisions regarding hormone therapy for managing menopausal symptoms.

Key takeaway

This multi-database study suggests that women using CE/BZA may have a slightly higher risk of endometrial cancer and hyperplasia but a lower risk of breast cancer compared to those using estrogen/progestin. Because for most women breast cancer presents a larger risk than endometrial cancer, CE/BZA shows promise as a safer alternative for hormone therapy, offering lower breast cancer risk with risks of other health outcomes. This provides valuable insights for healthcare providers and patients in making informed hormone therapy choices.

Read the complete study published in
Menopause: The Journal of The North American Menopause Society
carelon.research/hormone-replacement-study

Contact us at
rwe@carelon.com

Learn more at
carelonresearch.com

Follow us on
LinkedIn

carelon®

Carelon Research
123 Justison Street, Suite 200, Wilmington, DE 19801
302-230-2000