A counterfactual approach to minimize channeling bias in post-market safety surveillance

Julia C Pitino[1], Jennifer M Polinski[1], Brenda Hinman-McIlroy[2], Michael C Snabes[2], Dionna Attinson[1], Stephanie E Chiuve[2]

[1]Aetion, Inc, New York, NY; [2]AbbVie, Inc, North Chicago, IL

For questions regarding this poster, please contact the corresponding author, Stephanie Chiuve (stephanie.chiuve@abbvie.com).

Scan QR code to download an electronic version of this poster presentation 1716192 and other AbbVie ICPE 2021 Presentations. To obtain a QR code reader, go to your device app store and search for "QR code reader."

Background & Objective

- Elagolix is an approved treatment for moderate to severe endometriosis (EM) pain, but its hypoestrogenic effects may increase risk of mood disorders.
- Prior evidence has found that EM pain is important risk factor for mood disorders in patients with EM. Additionally, elagolix initiators may have more severe EM pain than the general population of patients with EM.
- This channeling bias must be addressed in order to accurately quantify rates of adverse events in the indicated population and can help to contextualize on-treatment adverse event rates in the post-market setting.

Objective: Use retrospective, real-world data to generate an unexposed comparator group for elagolix users (counterfactual, or CF group) and quantify the rate of mood disorders in the counterfactual group relative to the general EM population (general EM group).

Methods

Study Population

- The overall EM cohort included women aged 15-55 with endometriosis (EM)or an elagolix prescription identified within the IBM MarketScan insurance claims database during the index period, starting July 1, 2018 and ending July 1, 2019.

Exposure:

- New initiation of elagolix, a product to treat EM-associated pain. New initiation was defined as the first elagolix prescription in the index period described above, with no prior use looking back over all data.

Study design

- The following mood disorders were defined: depression (by ICD diagnosis code or antidepressant Rx), anxiety (by ICD diagnosis code or antianxiolytic Rx) and suicidality/self harm (by ICD diagnosis code).
- The baseline period was defined as the 365 days prior to and including index date.
- Index date was new initiation of elagolix for exposed patients, and an EM diagnosis for unexposed patients.
- Patients were followed until the earliest of disenrollment, death, outcome event, one year maximum follow-up reached, or end of data (Sep 30, 2020).

Methods and Statistical analysis

- Patients from the overall EM cohort were sorted into those exposed and unexposed to elagolix.
- A propensity score to predict elagolix initiation was developed based on demographics, comorbidities and medication use over baseline.
- Women with EM unexposed to elagolix were matched 1:1 with a 1% caliper to exposed elagolix initiators, to generate a counterfactual (CF) group (N=1,206).
- Baseline characteristics were quantified among the general EM group (N=134,820) and CF group, as well as follow-up risk (per 1,000 patients) of adverse events.
- Significance of baseline prevalence and follow-up risk for mood disorders was assessed using Chi-squared and Fisher's exact tests.
- The relative risk (RR) (95%CI) of mood disorders during follow-up, comparing the counterfactual group and general EM group, was estimated.
- Data were analyzed using the Aetion Evidence Platform (AEP)®.

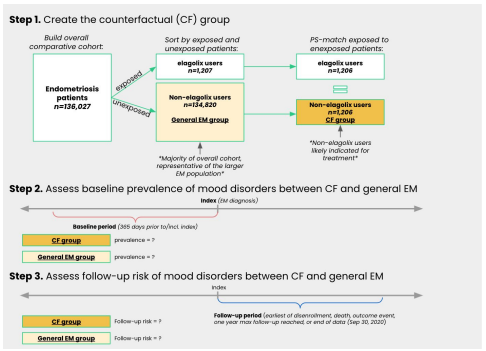

Figure 1. *Illustration for building of counterfactual (CF) group and study design.*

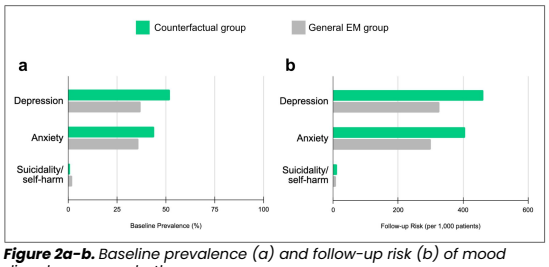

Figure 2a-b. *Baseline prevalence (a) and follow-up risk (b) of mood disorders among both groups.*

Results

Counterfactual vs General EM groups

- After PS matching, there were no significant differences among baseline covariates between the CF group (unexposed) and true elagolix users (exposed).
- At baseline, the prevalence of each mood disorder in the CF vs general EM group was (Fig. 2a):
  - 52% vs 37% for depression, 44% vs 36% for anxiety, 1% vs 2% for suicidality/self-harm.
- During follow-up, the risk per 1,000 women in the CF vs general EM group was (Fig. 2b):
  - 462 vs 327 for depression, 406 vs 301 for anxiety, 12 vs 9 for suicidality/self-harm.
- The RR (95% CI) comparing the CF vs general EM population was (Fig 3):
  - 1.42 (1.33, 1.50) for depression, 1.35 (1.26, 1.44) for anxiety, 1.34 (0.79, 2.27) for suicidality/self-harm.
- For all three mood disorders, there was significant correlation between baseline prevalence and follow-up risk (p-value <0.001).

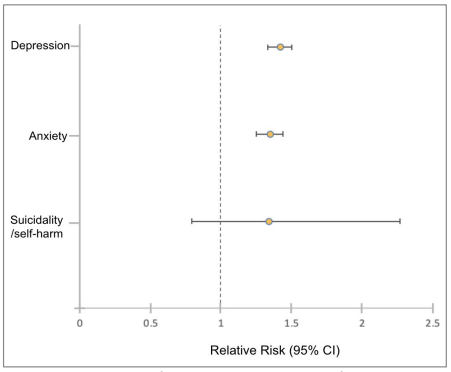

Figure 3. *Relative risks (95% CI shown by error bars) of mood disorders, comparing counterfactual (CF) and general endometriosis groups. Dotted line represents RR=1 (no increased risk for either group), right of line represents RR>1 (increased risk in CF group).*

Conclusions

Women with EM with clinical profiles similar to elagolix initiators may have a higher baseline risk of mood disorders relative to the general EM population. This difference could be a function of disease severity, as identified by their moderate to severe chronic pain compared to the general EM population which may have milder symptoms. Higher baseline risk of mood disorders may be associated with, and account for, increased risk during follow-up. Overall counts of suicidality/self-harm were low in both groups, due to the limitations of capturing this condition in claims data. Future work could explore an alternate or proximal definition for the condition, such all severe mood disorders.

Disclosure

This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication. This work was done under a contract between Aetion and AbbVie.
BHM, MCS, and SEC are employees of AbbVie receiving stock and/or stock options in AbbVie Inc.. JCP, JMP and DNA are employees of Aetion, Inc receiving stock and/or stock options in Aetion Inc.