

## ASSESSING RESIDUAL BIAS WITHIN A REAL-WORLD ANALYSIS A PRIORI: A CASE STUDY OF CARDIOVASCULAR (CV) RISK PROFILE IN INDIVIDUALS TREATED FOR OVERACTIVE BLADDER (OAB)

### Hypothesis / aims of study

Mirabegron (Myrbetriq/Betmiga; Astellas Pharma) is a  $\beta_3$  adrenergic receptor agonist with demonstrated efficacy and safety at managing the symptoms of OAB.<sup>1</sup> In clinical practice, mirabegron is typically given as second-line pharmacotherapy, after failure or dissatisfaction with antimuscarinics.<sup>2</sup> To date, the efficacy of mirabegron has been assessed in a number of randomized controlled trials, but limited safety information is available based on analysis of large sample sizes in a real-world observational setting. Integrated claims and electronic health records (EHR) datasets can be powerful research tools due to availability of detailed clinical data and ability to corroborate findings across datasets. However, comparisons of endpoints between groups may be affected by residual bias due to unmeasured confounding. This is particularly relevant when comparing medications typically administered sequentially for the same indication, as inherent patient differences can lead to identification of spurious associations. Falsification analysis, in which endpoints with no known association to treatment are identified and compared, is a recently proposed technique for assessing residual bias.<sup>3</sup> If unassociated outcomes appear to be associated with treatments under study, further analysis should be stopped to avoid biased findings.

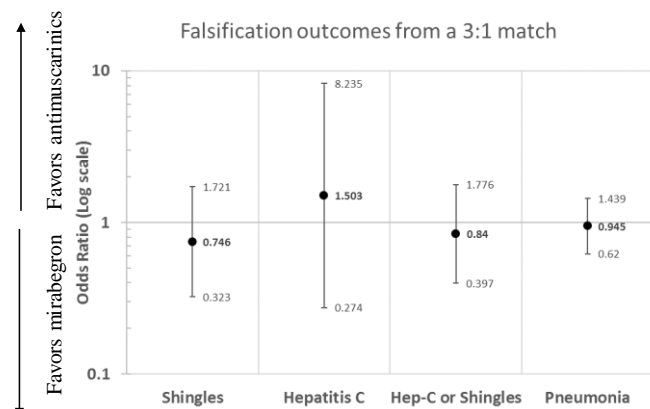
The objective of this study was to assess presence of residual bias via a falsification endpoint analysis of OAB patients treated with mirabegron or antimuscarinics.

### Study design, materials and methods

Claims and EHR data of OAB patients were examined. Index date was defined as the first date of treatment using antimuscarinics or mirabegron between October 2012 and December 2014. Unadjusted patient characteristics, including CV risk factors, were compared across groups at index and propensity-matching was used to reduce bias associated with observed confounders. A 3:1 propensity matching scheme was employed to improve efficiency given a relatively small number of mirabegron patients available in the dataset relative to antimuscarinic patients. Falsification analysis was used on the propensity-matched cohort to assess the associations between OAB treatment and outcomes with no known relationship to OAB treatment. Falsification analysis is characterized by odds ratios and corresponding 95% confidence intervals (CI) between treatment groups. The chosen falsification endpoints were hepatitis C, shingles, and community-acquired pneumonia, and a combined endpoint of hepatitis C and shingles, all of which have no known or plausible relationship with the exposure or outcome of interest.

### Results

10,311 antimuscarinic patients and 408 mirabegron patients were identified. Compared to AM patients, mirabegron patients were older (mean age 70 vs. 67 years), more likely to be male, to have had a recent CV event, and/or to have other comorbidities. After 3:1 propensity-matching, the sample included 1,188 antimuscarinic patients and 396 mirabegron patients; no statistically significant baseline differences were observed between treatment groups in the matched sample. Point estimates and 95% CIs for falsification endpoint odds ratios for mirabegron relative to antimuscarinics were 0.7 (CI: 0.3-1.7) for shingles, 1.5 (CI: 0.3-8.2) for hepatitis C, 0.8 (CI: 0.4-1.8) and 0.9 (CI: 0.6-1.4) for pneumonia (Figure). While 95% CIs spanned 1.0, all were wide due to small sample sizes; and hence definitive conclusions could not be drawn and the presence of residual bias could not be excluded.



Hep-C=Hepatitis C

### Interpretation of results

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### Concluding message

In a real world analysis, baseline risk for CV events differs between OAB patients receiving mirabegron versus antimuscarinics. While propensity matching was successful at balancing known covariates, a small sample size and resultant wide CIs for falsification analysis was concerning, as such the potential for residual bias could not be ruled out.

### References

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### Disclosures

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