**BACKGROUND**

- Hypercholesterolemia (HC) is a common chronic disorder sometimes requiring multiple treatments.
- The first-line treatment for HC is a statin, but some patients also require the addition of a second treatment to control or slow disease progression.¹
  - Ezetimibe, an inhibitor of intestinal cholesterol (and related phytosterol) absorption, is a common add-on for HC.
  - Colesevelam is a unique bile acid sequestrant indicated as an adjunct to diet and exercise to reduce elevated low-density lipoprotein cholesterol (LDL-C) in adults with primary hyperlipidemia, and to improve glycemic control in patients with type 2 diabetes; it is another approved add-on therapy for HC.
  - Ezetimibe or colesevelam can be used as monotherapy if warranted, especially in cases of statin intolerance.
  - Evidence regarding real-world treatment patterns for stool-bound agents is lacking.

**OBJECTIVE**

To examine prevalence of concomitant statin use and associated factors among hypercholesterolemia patients newly treated with ezetimibe or colesevelam.

**METHODS**

- Retrospective analysis of healthcare claims.
- Claims for services occurring January 1, 2009—July 31, 2012 were observed.
- Concomitant statin use was identified by a pharmacy claim for a statin within 3 months after the first pharmacy claim for ezetimibe or colesevelam.

**SAMPLE**

Study subjects were identified via the following criteria:

- Inclusion Criteria:
  1. A pharmacy claim for ezetimibe or colesevelam (‘target medication’). The date of the first pharmacy claim during this period was used as the index date.
  2. At least 2 pharmacy claims for the target medication where the second claim occurs within 60 days of the expected fill date (service-date plus days of supply) of the first claim.
  3. Diagnosis of pure hypercholesterolemia was required.
  4. Both medical and prescription drug coverage for the subject.
  5. Subject age 18–90 years as of the index date.
  6. Continuous enrollment for 180 days pre-index through 360 days post-index. A gap in coverage 31 days was allowed for inclusion exclusion.

- Exclusion Criteria:
  1. Pharmacy claims for the target medication during the 6-month pre-index period (wash-out).
  2. Pharmacy claim for multiple different target medications during the 18-month observation period.
  3. Any medical claims with a primary or secondary diagnosis code for pure hypercholesterolemia, mixed hyperlipidemia, or any hyperlipidemia.
  4. Enrolment at any time during the observation period in a plan with contractual exclusions from research.

**RESULTS**

**RESULTS SUMMARY**

- Sample size consisted of 679 colesevelam and 1439 ezetimibe patients, after applying all inclusion/exclusion criteria.
- Similar baseline characteristics were observed across the 2 groups (see Table 1).
- Concomitant use of statins was 24% among colesevelam and 50% among ezetimibe patients, respectively (see Table 2).
- After adjustment for patient demographics and comorbidities (see Table 3), ezetimibe patients were 3.2 times more likely than colesevelam patients to have concomitant statin use (OR = 3.146, 95% CI: 2.573, 3.960, p<0.001).
- Other significant factors associated with higher concomitant statin use include:
  - Male gender (OR = 1.766, 95% CI: 1.558, p<0.001).
  - Presence of diabetes mellitus (OR = 1.002, 95% CI: 1.003, 1.135, p<0.001).
  - Higher Type-2 Charlson Comorbidity Index (OR = 1.114, 95% CI: 1.046, 1.187, p<0.001).

**LIMITATIONS**

- Concomitant use of statins was more frequent with ezetimibe than colesevelam.
- Disproportionate concomitant statin use should be accounted for when comparing outcomes of patients taking ezetimibe versus colesevelam.
- Further research is needed to determine the causes of disproportionally concomitant statin use among ezetimibe and colesevelam patients which may include statin intolerance or for other safety/holistic concerns.

**REFERENCES**


**ACKNOWLEDGMENTS**

Special thanks to:
Karan Moll, PhD, Comprehensive Health Insights for analytical assistance
Rajiv Mallick, PhD, Daiichi Sankyo for contributions to post-derogation.

**CONCLUSIONS**

- Significant comorbidities common to patients using ezetimibe and colesevelam.
- The results are consistent with the 2013 JAMA study reported by the same research team but extended to 2012.
- There is a need for additional research on the integration of ezetimibe colesevelam in clinical practice.

**CONSORT**

- CONSORT (Consolidated Standards of Reporting Trials).
- CONSORT for claims data studies.
- The CONSORT team revisited the 2010 guidelines to develop recommendations for claims data studies.

**ANALYSIS**

- Concomitant Statin Use with Ezetimibe or Colesevelam for Treatment of Hypercholesterolemia
- Xin Ye, PhD; Harold Bayes, MD; Phil Schwab, MS; Anthony Louder, PhD
- Daiichi Sankyo, Parsippany, NJ; 2Louisville Metabolic and Atherosclerosis Research Center, Louisville, KY; 3Comprehensive Health Insights a Humana company, Louisville, KY

**Table 1 - Baseline group descriptive statistics**

<table>
<thead>
<tr>
<th></th>
<th>ezetimibe</th>
<th>colesevelam</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion n</td>
<td>726</td>
<td>1,439</td>
<td></td>
</tr>
<tr>
<td>Gender: Female (%)</td>
<td>43.6% (627)</td>
<td>43.6% (627)</td>
<td>0.947</td>
</tr>
<tr>
<td>Region: Northeast (%)</td>
<td>2.4% (16)</td>
<td>2.4% (16)</td>
<td>0.913</td>
</tr>
<tr>
<td>Age mean (95% CI)</td>
<td>67.5 (67.0, 68.0)</td>
<td>66.6 (65.8, 67.4)</td>
<td>0.0058</td>
</tr>
<tr>
<td>Hyperlipidemia (n)</td>
<td>78.6% (1,094)</td>
<td>79.3% (1,092)</td>
<td>0.621</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>62.1% (879)</td>
<td>62.1% (879)</td>
<td>0.997</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus (n)</td>
<td>33.2% (477)</td>
<td>36.1% (502)</td>
<td>0.136</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>5.9% (101)</td>
<td>5.9% (101)</td>
<td>0.997</td>
</tr>
</tbody>
</table>

**Table 2 - Concomitant Statin Use: Unadjusted Comparison**

<table>
<thead>
<tr>
<th></th>
<th>ezetimibe</th>
<th>colesevelam</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concomitant Use vs –</td>
<td>Yes</td>
<td>No</td>
<td>p = 0.0001</td>
</tr>
<tr>
<td>Concomitant Statin Use –</td>
<td>Yes</td>
<td>No</td>
<td>p = 0.0011</td>
</tr>
</tbody>
</table>

**Table 3 - Concomitant Statin Use: Adjusted Comparison**

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender: Male vs Female</td>
<td>1.296</td>
<td>(1.079, 1.558)</td>
<td>0.0056</td>
</tr>
<tr>
<td>Region: West vs Northeast</td>
<td>1.000</td>
<td>(0.949, 1.049)</td>
<td>0.0491</td>
</tr>
<tr>
<td>Region: Midwest vs Northeast</td>
<td>1.000</td>
<td>(0.993, 1.007)</td>
<td>0.4668</td>
</tr>
<tr>
<td>Region: South vs Northeast</td>
<td>1.018</td>
<td>(0.808, 1.311)</td>
<td>0.1495</td>
</tr>
<tr>
<td>Ezetimibe-Colesevelam Index</td>
<td>1.114</td>
<td>(1.046, 1.187)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>1.262</td>
<td>(1.035, 1.539)</td>
<td>0.0212</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.111</td>
<td>(0.940, 1.316)</td>
<td>0.0827</td>
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<tr>
<td>Hypertension</td>
<td>1.080</td>
<td>(0.863, 1.352)</td>
<td>0.5002</td>
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