Mortality and Hospitalization Following Initiation of Sacubitril/Valsartan in the Medicare Population

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Disclosures
• All authors report no conflicts of interest.

Background
• Sacubitril/valsartan was approved in 2015 for treatment of chronic heart failure with reduced ejection fraction (HFrEF).
• Few population-based studies have characterized early users of this medication.

Objectives
• To describe a population-based cohort of patients initiating sacubitril/valsartan in terms of their baseline characteristics and subsequent clinical outcomes.

Methods
• Study design: Retrospective cohort of new users of sacubitril/valsartan in 2015-2016
• Data source: 20% sample of Medicare administrative claims records from 2007-2016
• Index date: First date of sacubitril/valsartan prescription.
• Inclusion criteria:
  • At least 1 prescription for sacubitril/valsartan.
  • Continuous Medicare Part A/B coverage for at least 1 year prior to index date.
  • Medicare Part D coverage on index date.
• Exclusion criteria:
  • Death or HF hospitalization on index date.
  • Baseline period: From 1/1/2007 or start date of Part A/B coverage, whichever occurred later, through the index date.
  • Follow-up period: From index date to the earliest of: endpoint of interest, loss of Part A/B/D coverage, death, or 12/31/2016 (separately for each endpoint).

Results

Table 1. Baseline characteristics of Medicare beneficiaries (2007-2016) initiating treatment with sacubitril/valsartan.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=4,111</th>
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<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>72.0 (10.9)</td>
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<tr>
<td>Female sex, N (%)</td>
<td>1,358 (33.0%)</td>
</tr>
</tbody>
</table>
| Race, N (%) | White 3,283 (79.8%)
  | Black 570 (13.9%)
  | Other 258 (6.3%) |
| Any HF diagnosis, N (%) | 4,091 (99.5%)
| Years since first HF diagnosis, mean (SD) | 5.0 (3.2)
| Any HF/EF diagnosis, N (%) | 3,783 (92.0%)
| Comorbid condition history, N (%) | Hypertension 3,997 (97.2%)
  | Diabetes 2,523 (61.3%)
  | Atrial fibrillation 2,389 (58.1%)
  | Hospitalization for HF 1,078 (26.2%)
  | Myocardial infarction 2,201 (53.5%)
  | Cerebrovascular disease 1,751 (42.6%)
  | Peripheral vascular disease 2,860 (69.6%)
  | Chronic pulmonary disease 2,606 (63.4%)
  | Renal disease 1,945 (47.3%)
| Recent prescriptions, N (%) | Angiotensin-converting enzyme inhibitor 49/51 mg 1,214 (29.5%)
  | Angiotensin II-receptor blocker 795 (19.5%)
  | Diuretic 2,877 (70.0%)
  | Beta-blocker 3,583 (87.2%)
  | Mineralocorticoid-receptor antagonist 1,512 (36.8%)
  | Sacubitril/valsartan dose at index | 24/26 mg 2,602 (63.3%)
  | 49/51 mg 1,185 (28.8%)
  | 97/103 mg 324 (7.9%) |

Figure 2. Cumulative incidence and 95% confidence interval (CI) of clinical events after initiation of sacubitril/valsartan.

Figure 1. Study design for example patient.

Baseline characteristics:
• Demographics: Identified from enrollment records
• HF/HFrEF: Defined by having a diagnosis on ≥1 claim from any source.
• Comorbid conditions: Defined by having a diagnosis on ≥1 inpatient or ≥2 outpatient claims on different days.
• Recent medications: Defined by having medication supply available on or within 30 days prior to the index date.

Outcomes:
• Discontinuation: A 45-day refill gap after the end of supply of the most recent fill.
• All-cause mortality: Death via linkage to the National Death Index.
• Cardiovascular (CV) death: Disease of the circulatory system (ICD-10: I00-I99) as the underlying cause of death.
• HF hospitalization: Hospitalization with HF as the primary discharge diagnosis.

Statistical Analysis:
• Cumulative probabilities of clinical outcomes estimated using the cumulative incidence competing risk method.
• Event rates and 95% confidence intervals estimated using Poisson regression.

Conclusions
• For the sacubitril/valsartan users in this cohort:
  • There was a high baseline comorbidity burden.
  • Rates of hospitalization and mortality were high, and 2/3 of deaths were attributable to CV causes.
  • Discontinuation of sacubitril/valsartan therapy was common.
• The Medicare 20% sample with linkage to the National Death Index represents a valuable tool for examining the effectiveness and safety of sacubitril/valsartan therapy.