Utilisation and Tolerability of Aliskiren; Final Results of a Prescription-Event Monitoring Study

Claire Doe1,2, Carole Fogg1, Deborah Layton1,2, Saad AW Shakir2
1Drug Safety Research Unit, Southampton, United Kingdom; 2University of Portsmouth, Portsmouth, United Kingdom

BACKGROUND

The renin inhibitor aliskiren (Rasilez®) is licensed for essential hypertension and was launched in the UK in Aug 2007. In clinical trials diarrhoea was a common ADR but angioedema (a known ADR with other Renin Angiotensin System drugs), occurred rarely. As aliskiren is first in its class, a Prescription-Event Monitoring (PEM) study was performed.

OBJECTIVE

To describe the utilisation characteristics and tolerability of aliskiren in patients in England under real life primary care conditions.

METHODS

This was an observational single exposure prospective cohort study. (See Figure 1)

Figure 1. Process of Prescription-Event Monitoring study

- DSRU notifies NHS Prescription Services (NHSRxS) of aliskiren PEM study.
- Prescriptions dispensed February 2008 - November 2010 for aliskiren identified.
- Details of patients and prescribing GPs sent to DSRU (exposure data collected).
- PEM questionnaires (Green Forms) sent to GPs (≥6 months after 1st prescription issued for patient).
- Outcome data requested includes: age, sex, treatment start/stop dates, dose, events*, reasons for stopping, adverse events, suspected ADRs and causes of death.
- Questionnaires returned, reviewed and data entered onto database.
- Selected events of medical interest, deaths (where cause not known) and pregnancies were followed-up.
- Causality Assessment of events followed-up.
- Summary descriptive statistics.

Percentages presented exclude patients where data was missing due to answers not being known or not being specified.

*An ‘event’ in PEM, is defined as, “any new diagnosis, any reason for referral to a consultant or admission to hospital, any unexpected deterioration (or improvement) in a concurrent illness, any suspected drug reaction, any alteration of clinical importance in laboratory values, or any other complaint that was considered of sufficient importance to enter in the patient’s notes.”

Figure 2. Age Sex Distribution of Final Cohort

Table 1. Most frequently reported primary indications (top 10)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number</th>
<th>% of cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>5958</td>
<td>93.3%</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
<td>68</td>
<td>1.1%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>48</td>
<td>0.8%</td>
</tr>
<tr>
<td>Intolerance to previous drug</td>
<td>39</td>
<td>0.7%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>19</td>
<td>0.3%</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>9</td>
<td>0.2%</td>
</tr>
<tr>
<td>Nephrotic Syndrome</td>
<td>4</td>
<td>0.1%</td>
</tr>
<tr>
<td>Cardiac Failure</td>
<td>12</td>
<td>0.2%</td>
</tr>
<tr>
<td>Inadequate response to previous drug</td>
<td>14</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Dose

Starting dose was 150mg as per SPC in 89.7% (5389/6007). Aliskiren was reported to have been effective in 77.4% (3888/5024).

ADRs

GPs were invited to indicate any events they felt were ADRs. Commonest specified ADRs:

- Diarrhoea (7.2%, 26/362)
- Malaise (6.4%, 23/362)

ADRs of Angioedema and Oedema face were uncommon. (Each 0.6%, 2/362).

Therapy Cessation

Aliskiren was stopped in 31.0% (1858 / 5995). There were 2388 reasons for stopping (RFS) in 1829 patients. Commonest RFS were:

- Not effective (16.6%, 397 / 2388)
- Diarrhoea (5.2%, 123 / 2388)

Angioedema was an uncommon RFS. (0.2%, 5 / 2388).

Deaths

There were 100 deaths during the study (1.6% of cohort). Where cause of death was specified, the majority were cardiovascular in nature, (44.7%, 34 / 76) followed by neoplasms (18.4%, 14 / 76).

CONCLUSIONS

Aliskiren was prescribed for hypertension in the vast majority of patients. Off label use was infrequent. Angioedema was an uncommon ADR and was uncommonly a RFS. Aliskiren was well tolerated but diarrhoea that was uncommonly a RFS in clinical trials, was a common RFS in this cohort.