Abstract: P4784

Efficacy and safety of dronedarone by duration of atrial fibrillation history: a post-hoc analysis of the ATHENA trial

Authors:
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Topic(s):
Atrial Fibrillation - Treatment

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Background: Atrial fibrillation (AF) is known to progress over time and the effectiveness of antiarrhythmic therapy may vary based on the duration of a patient's AF history. Outcomes with dronedarone (DRO) based on duration of AF/atrial flutter (AFL) history have not been previously characterized.

Purpose: To evaluate the efficacy and safety of DRO by time since first known AF/AFL episode in patients studied in the ATHENA trial.

Methods: 2859 (61.8%) patients from ATHENA with documented first known AF/AFL episode (of 4628 total patients randomized) were included in the analysis. Among these patients, first AF/AFL episode was reported at <3 months (shorter history), 3 to <24 months (intermediate), and ≥24 months (longer) in 1296 (45.3%), 845 (29.6%) and 718 (25.1%) patients, respectively. AF/AFL recurrence was evaluated in patients in sinus rhythm at baseline by ECG during study visits or symptom recurrence.

Results: Demographics (age, sex) were similar across all groups. Patients with longer AF/AFL history tended to have higher prevalence of coronary heart disease and structural heart disease; and were more likely to have AF/AFL (by 12-lead ECG) at baseline (30%) compared to 26% and 16% for intermediate and shorter history groups. Patients with a longer AF history likely had a prior ablation for AF/AFL (7%) vs patients with an intermediate (2%) or shorter AF/AFL history (1%), and more likely required cardioversion during the study (24%) vs intermediate (17%) and shorter history groups (11%). Outcomes and efficacy are reported in Table 1. Rates of treatment-emergent adverse events (TEAEs), serious TEAEs, permanent drug discontinuations, and deaths were similar across all AF/AFL groups.

Conclusions: Nearly half the patients in ATHENA had a shorter history (<3 months) of AF/AFL prior to randomization. Patients with a longer history of AF/AFL had a greater burden of AF/AFL based on baseline rhythm status, ablation history, and cardioversions required post randomization. Despite these differences, clinical outcomes, efficacy, and safety of DRO appeared to be generally consistent irrespective of duration of AF/AFL history.

Table 1. Outcomes and efficacy summary

<table>
<thead>
<tr>
<th>Relative Risk, dronedarone (DRO) vs placebo (PBO)1 (95% CI)1,2</th>
<th>AF/AFL &lt;3 months</th>
<th>AF/AFL 3 to &lt;24 months</th>
<th>AF/AFL ≥24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO (n=626)</td>
<td>DRO (n=670)</td>
<td>PBO (n=429)</td>
<td>DRO (n=416)</td>
</tr>
<tr>
<td>First CV hospitalization2 or death (any cause)</td>
<td>0.79 (0.65, 0.96)</td>
<td>0.72 (0.56, 0.92)</td>
<td>0.84 (0.66, 1.07)</td>
</tr>
<tr>
<td>First CV hospitalization</td>
<td>0.78 (0.64, 0.96)</td>
<td>0.70 (0.55, 0.91)</td>
<td>0.82 (0.63, 1.05)</td>
</tr>
</tbody>
</table>

1Cox regression model.

2On study period, all randomized patients.

3Main reason was AF/other supraventricular rhythm disorders.

4On selected patients in sinus rhythm at baseline (AF/AFL <3 months: PBO n=514, DRO n=529; 3 to <24 months: PBO n=288, DRO n=312; ≥24 months: PBO n=252, DRO n=250). CV = Cardiovascular.
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<th>Event</th>
<th>DRO (n=670)</th>
<th>PBO (n=626)</th>
<th>DRO (n=416)</th>
<th>PBO (n=429)</th>
<th>DRO (n=355)</th>
<th>PBO (n=363)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (any cause)</td>
<td>0.82 (0.54, 1.24)</td>
<td>0.85 (0.43, 1.68)</td>
<td>1.13 (0.61, 2.10)</td>
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<tr>
<td>First AF/AFL recurrence</td>
<td>0.80 (0.65, 0.97)</td>
<td>0.67 (0.53, 0.84)</td>
<td>0.81 (0.65, 1.02)</td>
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