Toxicity and therapeutic efficacy of standard and reduced amiodarone maintenance dosing

Stephanie A. Dougherty, PharmD; Kristen Bova Campbell, PharmD, BCPS (AQ Cardiology), CPP; Albert Sun, MD
Duke University Hospital; Durham, North Carolina

Background

Amiodarone Effectiveness vs. Side Effects
- Amiodarone demonstrates efficacy in all forms of supraventricular and ventricular tachycardias
- Use of amiodarone is often limited by adverse effects, including end organ toxicity, which can lead to therapy discontinuation
- Thyroid abnormalities 1-10%, Liver toxicity 3-9%, lung toxicity 1-17% 1-4
- The Electrophysiology department at Duke has lowered maintenance doses in some patients who are clinically stable

Objectives

Primary Objective
- To determine the combined event rate of amiodarone toxicity (thyroid toxicity, hepatotoxicity, and pulmonary toxicity), and failure* between two amiodarone dosing regimens (standard dose vs reduced dose) for patients with any arrhythmia in the Duke University Health System
- *Failure: amiodarone discontinuation or incidence of ablation

Secondary Objectives
- To compare the absolute incidence of combined toxicity (thyroid, liver, or lung toxicity) between the standard and reduced amiodarone dosing groups after 6 and 12 months of therapy
- To compare the incidence of amiodarone failure between the standard and reduced amiodarone dosing groups after 6 and 12 months of therapy

Study Design
- Retrospective, multisite (Duke University Hospital, Duke Regional Hospital, Duke Raleigh Hospital) cohort review
- All potential subjects for inclusion will be identified via a query of the Duke Enterprise Data Unified Content Explorer (DEDUCE) and Epic Maestro Care databases based on amiodarone initiation
- Incidence of major side effects highly variable
- Adverse effects generally related to dose and duration of therapy
- Lower maintenance dose of amiodarone may lead to fewer side effects

Data Collection

The following information will be obtained from DEDUCE and electronic medical records:
- Patient demographics (age, gender, race) and pertinent PMH
- Indication for amiodarone
- Initial maintenance dose of amiodarone and date initiated
- Date of amiodarone dose change
- New amiodarone dose if dose changed and reason for change
- Any available TSH levels, ALT and AST levels, and PFTs following amiodarone initiation until event, loss of contact with patient, or end of study period
- Occurrence of ablation procedure completed within the study time frame following initiation of amiodarone, and date of ablation
- Any discontinuation of amiodarone therapy following initiation and date of discontinuation
- Date of amiodarone related event (toxicity found, ablation done, or amiodarone discontinued)
- If patient remains on dose, date when last contact, or last known date patient was stable

Methods

Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 18 years at time of amiodarone initiation</td>
<td>Incomplete medical record documentation</td>
</tr>
<tr>
<td>Documented diagnosis code of atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, or ventricular fibrillation</td>
<td></td>
</tr>
<tr>
<td>Prescribed amiodarone at a dose of 100 mg, 200 mg, or 400 mg per day</td>
<td></td>
</tr>
<tr>
<td>Documented baseline TSH panel</td>
<td></td>
</tr>
<tr>
<td>Documented baseline LFT panel</td>
<td></td>
</tr>
<tr>
<td>Experience one event of interest within 12 months of starting a maintenance dose or stay on a given dose for at least 12 months</td>
<td></td>
</tr>
</tbody>
</table>

Sample Size
- It is estimated that approximately 860 patients will meet study inclusion criteria

Statistical Considerations

Primary Endpoint
- Combined event rate of thyroid toxicity, hepatotoxicity, pulmonary toxicity, amiodarone discontinuation, or ablation in each dosing group

Secondary Endpoints
- Absolute incidence of clinical hypothyroidism
- Absolute incidence of hepatotoxicity
- Absolute incidence of pulmonary toxicity
- Absolute Incidence of amiodarone discontinuation
- Absolute incidence of ablation

Sample Size
- It is estimated that approximately 860 patients will meet study inclusion criteria

Statistical Analysis
- Incidence rates within each dosing group will be presented using counts and percentages using only subjects who have the event of interest or stay on a given maintenance dose for the time point of interest (i.e. 6 or 12 months)
- Pairwise comparisons between standard and reduced dose groups will be done using a Chi-Square or Fisher’s exact test to compare incidence rate of any type of toxicity, ablation, or amiodarone discontinuation

References

Disclosures
Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
- Stephanie A. Dougherty, PharmD: Nothing to disclose
- Kristen Bova Campbell, PharmD: Nothing to disclose

This study has been approved by the Duke Health System Institutional Review Board. Data collection is in progress.