Irbesartan in patients with heart failure and preserved ejection fraction

Study Type: POEM
Purpose: Whereas 50% of patients with HF have preserved ejection fraction and the rate of death and illness in these patients is high and is often associated with older females, no pharmacologic therapy has been shown to reduce outcomes. This study assesses the use of irbesartan in these patients on CV outcomes.

Study Duration: 5 years, mean follow-up of 50 months
Trial Design: Randomized, double-blinded, intention-to-treat, multicenter (293 centers, 25 countries). Used a 1 to 2 week placebo run-in phase to assess compliance. Patients could be on an ACE inhibitor.

Medications: Irbesartan 75 mg vs placebo, increased to 150 mg and then to 300 mg every 2 weeks

Patients: n = 4128, mean age 72, 60% female, 93% white, 2% black, 76% Class III, EF = 60%, BMI 29, 64% was caused by HTN, BP = 136/80, 44% had been hospitalized in previous 6 mths, SCr 1.0, Minnesota QOL 42 (score ranges 0 to 105, lower scores indicated a better QOL)

Medication: Diuretics 84%, Spironolactone 15%, ACEI 25%, Digoxin 13%, BB 58%, CCB 40%, Nitrate 27%, Warfarin 19%, Antiplatelet 58%, Lipid drug 30%

Past events: HTN 88%, MI 23%, angina symptoms 40%, a. fib 29%, diabetes 27%, stroke 10%, revascularization. 13%

Inclusion Criteria: > 60 years of age, HF symptoms with EF of at least 45%, had to be admitted to hospital for HF symptoms during the previous 6 mths and classed as NYHA class II, III or IV, they took class III/IV with evidence but did not require hospitalization

Exclusion Criteria: EF < 40%, other explanation of HF (pulmonary HTN), a history of ACS, or revascularization, or stroke within 3 months of enrollment, + loads of other exclusions too numerous to list here - see study

Primary outcome: time to first event of death from all causes + hospitalization for a CV cause

Secondary outcome: Components of primary outcome, heart failure outcomes, quality of life + others

1. Are the results valid?
   * Randomized? Yes Similar groups? Yes
   * Double-blinded? Yes Allocation concealment? ?
   * Placebo-controlled? Yes Patient accountability? Yes

2. What were the results?

<table>
<thead>
<tr>
<th>Primary outcome with Components</th>
<th>Irbesartan</th>
<th>Placebo</th>
<th>P-value</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death all cause + hospitalization for CV cause</td>
<td>36%</td>
<td>37%</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All death</td>
<td>10.7%</td>
<td>10.9%</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization for CV causes</td>
<td>25%</td>
<td>26%</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* All other secondary outcomes were not significant – worsening HF, MI, unstable angina, stroke, arrhythmia, death from CV causes, all cause hospitalization
* Both groups improved on the Minnesota QOL assessment, no difference in improvement between groups
* Subgroup analysis made no difference (e.g., if had diabetes or not, EF, sex, use of ACEI or BB, etc.)

3. Will the results help me?
   * No difference in adverse events between groups, ~14% discontinued drug in either group
   * Reasons for lack of benefit – dose is too low, mis-diagnosis (authors felt like they had minimized this problem), high rate of ACEI use in placebo group (~40%), high rate of spironolactone use in placebo group (29%), use of Beta-blocker in each group (73%), other studies have shown a lack of benefit.

Conclusion: Irbesartan did not reduce the risk of death or hospitalization for CV causes among patients with HF with a preserved EF, nor did it improve QOL.