Pharmacogenetic Guided β-Blocker Therapy with Bucindolol for the Prevention of Atrial Fibrillation/Flutter in Heart Failure: Relationship of Left Ventricular Ejection Fraction to Treatment Effect

Background

- There are very few guideline-recommended antiarrhythmic drugs for atrial fibrillation (AF) or atrial flutter (AFL) in heart failure (HF) and those that are recommended carry risks of end-organ toxicities and/or proarrhythmias.

- Bucindolol hydrochloride (bucindolol) is a nonselective β-blocker with two unique pharmacologic properties:
  - Sympatholysis: decreases adrenergic drive/norepinephrine release.
  - Inverse agonism: inhibition of constitutively active β-receptors.

- The BEST Trial was approved by the Treatment Panel for the prevention of AF recurrence, a differential response in patients with different genotypes to bucindolol.

- For the prevention of AF recurrence, bucindolol response was examined in patients with different left ventricular ejection fraction (LVEF) levels.

- The goal of the GENETIC AF Trial was to compare the effects of pharmacogenetically targeted bucindolol to the standard of care in a genotype-defined, randomized HF population at high risk of AF/AFL recurrence.

β-AR Polymorphisms

- The β3/2 LVEF 0.37 – 2.9 LVEFs are presented unless otherwise specified.

Patient Baseline Characteristics

- As shown in Figure 6, the restriction of the population to higher LVEF was associated with increasing bucindolol response (OR: 0.96, CI: 0.93, 0.99).

- As shown in Table 3, a trend for greater bucindolol response in patients with lower LVEF was associated with increasing bucindolol response (OR: 0.61, CI: 0.48, 0.80).

Conclusions

- For the prevention of AF recurrence, bucindolol response may be lower in patients with lower LVEF values.

- The best blocker therapy may be less desirable in patients with lower long-standing HF and/or AF, due to an inability to modify substrate in advanced stages of heart disease.

References


