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**Presentation Number:** 410-16  
**Topic 1:** Heart Failure and Cardiomyopathies  
**Patients Enrolled:** 8256  
**Published Acronym:** GALACTIC-HF  
**Published Name of Trial:** Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure

**Trial Type:** Secondary analysis of major clinical trial  
**Publishing Title:** Impact Of Ejection Fraction On The Therapeutic Effect Of Omecamtiv Mecarbil In Patients With Heart Failure And Reduced Ejection Fraction: A Secondary Analysis From GALACTIC-HF

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**Background:** Omecamtiv mecarbil, a cardiac myosin activator, increases cardiac function and decreases left ventricular (LV) volumes and NT-proBNP in patients with heart failure with reduced ejection fraction (HFrEF). In GALACTIC-HF, omecamtiv mecarbil significantly reduced the primary composite endpoint (PCE) of time to first heart failure event or cardiovascular death in patients enrolled with LV ejection fraction  $\leq 35\%$ .

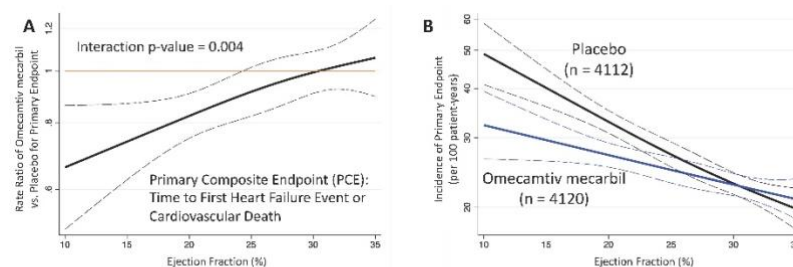
**Methods:** We evaluated the influence of EF on the therapeutic effect of omecamtiv mecarbil compared to placebo in 8,232 patients analyzed in GALACTIC-HF.

**Results:** Patients with lower EF were more likely to be younger, male, non-White, from the Americas or Western Europe, and to have ischemic HF etiology, NYHA III/IV, normal sinus rhythm, lower blood pressure, higher baseline NT-proBNP and troponin compared to those with higher EF. The most significant heterogeneity in the effect of omecamtiv mecarbil on the PCE was with respect to EF (continuous interaction,  $p = 0.004$ ).

Omecamtiv mecarbil had progressively greater improvement in the PCE with decreasing EF as demonstrated by the continuously improving rate ratio (Panel A). The incidence of the PCE increased with decreasing EF and omecamtiv mecarbil produced increasingly greater absolute reductions in the PCE with decreasing EF (Panel B).

**Conclusion:** Omecamtiv mecarbil exerts a greater relative and absolute therapeutic benefit with worsening EF, in keeping with the drug's mechanism of selectively improving cardiac function.

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Panel A: Treatment effects of omecamtiv mecarbil versus placebo across a range of ejection fractions for the PCE with estimated rate ratios and 95% confidence intervals. Panel B: Incidence of PCE in the Placebo (Black) and Omecamtiv mecarbil (Blue) groups across a range of ejection fractions with estimated rates and 95% confidence intervals. Difference between lines represents absolute rate reduction.