



# Drug Monitor

ONLINE EDITION

## Allopurinol Use and Heart Failure Morbidity and Mortality

Allopurinol as treatment for an elevated uric acid level could affect the risk of mortality and morbidity in patients with systolic heart failure, according to a recent study. After analyzing 1,152 patients with advanced heart failure, researchers say that elevated uric acid level and allopurinol use were independent predictors of high mortality and morbidity.

The patients were participants in the Prospective Randomized Amlodipine Survival Evaluation (PRAISE) study, which was conducted from 1992 to 1994. Inclusion criteria in the PRAISE study included New York Heart Association class IIIB or IV, and a left ventricular ejection fraction < 30% while on maximal medical therapy, including diuretics, digoxin, and angiotensin-converting enzyme

inhibitors. Researchers in the most recent study analyzed all PRAISE participants who had their uric acid level measured at study entry.

Participants were divided into 5 groups for analysis: those not treated with allopurinol, who were stratified into 4 quartiles of uric acid level (2.2 mg/dL to 7.1 mg/dL, > 7.1 mg/dL to 8.6 mg/dL, > 8.6 mg/dL to 10.4 mg/dL, and > 10.4 mg/dL); and those treated with allopurinol. Median follow-up time to first morbidity/mortality event or censoring was 404 days.

Patients taking allopurinol and nonallopurinol users in the highest quartile of uric acid level had the highest total mortality (41.7 and 42.4 per 100 person-years, respectively). These 2 groups also had the highest combined morbidity/mortality (45.6 and 51.0 per 100 person-years, respectively). According to researchers, allopurinol use was associated

with an approximately 65% increase in risk of death, while being in the highest uric acid level quartile was associated with a 35% increase in risk of death, compared with nonallopurinol users in the lowest uric acid level quartile.

The researchers caution against inferring a link between allopurinol use and adverse outcomes. For example, the pathogenesis of an elevated uric acid level in the patient with chronic heart failure has multiple factors, including impaired renal function and metabolic derangements, such as insulin resistance. Furthermore, since allopurinol is used to treat an elevated uric acid level, patients on allopurinol likely fell into the higher uric acid level quartiles. Rather, the researchers say, allopurinol use should be considered a risk marker in patients with heart failure. ●

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