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HEART FAILURE

Rolofylline fails to improve renal function in patients with acute HF

The adenosine A_1 receptor antagonist rolofylline does not prevent persistent worsening of renal function in patients with acute heart failure and volume overload, according to the results of PROTECT, a large, phase III clinical trial. This finding is unexpected and disappointing because "initial proof-of-concept studies and a 301-patient pilot study suggested that selective adenosine A_1 receptor antagonists could enhance diuresis while preserving or improving renal function in this high-risk population," reports Dr Michael Givertz, one of the trial investigators.

The researchers randomly assigned 2,033 patients to receive either rolofylline (30 mg) or placebo as a 4 h, intravenous infusion daily for 3 days. Persistent worsening of renal function (defined as an increase in serum creatinine ≥0.3 mg/dl at both days 7 and 14, or initiation of hemofiltration or dialysis, or death by day 7) was not different in the rolofylline group when compared with the placebo group (15.0% vs 13.7%, odds ratio 1.11, 95% CI 0.85–1.46, $P = 0.44$). Furthermore, in the primary end point analysis (published previously in the *New England Journal of Medicine*), rolofylline was associated with a higher risk of seizure, a known potential adverse effect of adenosine A_1 receptor antagonists.

The compound's lack of efficacy means that "further development of this class of agents is on hold until safer and more effective compounds are identified," says Dr Givertz.

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Original article Voors A. A. *et al.* Effects of the adenosine A_1 receptor antagonist rolofylline on renal function in patients with acute heart failure and renal dysfunction. Results from PROTECT (Placebo-controlled randomized study of the selective A_1 adenosine antagonist rolofylline for patients hospitalized with acute decompensated heart failure and volume overload to assess treatment effect on congestion and renal function). *J. Am. Coll. Cardiol.* **57**, 1899–1907 (2011)