Safety and tolerability of sacubitril-valsartan: a systematic review and meta-analysis

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ABSTRACT

Introduction: Sacubitril-valsartan is a recently approved drug. However, there are few data regarding safety issues. We aimed to summarize the available evidence regarding sacubitril-valsartan's safety and tolerability.

Methods: We conducted a systematic review with meta-analysis of randomized controlled trials (RCTs) enrolling patients receiving sacubitril-valsartan for any condition, compared with standard therapy or placebo. Database search was performed in October 2019. Outcomes were adverse events (AEs), serious AEs (SAEs), discontinuation due to AEs, and five AEs of special interest. Data were reported using risk ratio (RR) and 95% confidence interval (95%CI).

Results: We included 20 RCTs (22510 participants). When compared with active controls, there were no differences in SAEs (RR=0.93, 95%CI 0.86–1.01) and AEs (RR=1.00, 95%CI 0.97–1.03). However, sacubitril-valsartan resulted in an 8% risk reduction in discontinuation due to AEs (95%CI 0.85–0.99) and an increased risk of hypotension (RR=1.45, 95%CI 1.27–1.67). The risk of angioedema was higher with follow-ups greater than 12 months (RR=2.36, 95%CI 1.29–4.33). There were no further significant differences in the remaining AEs' risk.

Conclusions: Sacubitril-valsartan was at least as safe and tolerable as active control, with a similar need of administration cautiousness, except for a higher risk of hypotension. However, one should consider the study's limitations.