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Pooled analysis of the phase 3 REVIVE trials: randomised, double-blind studies to evaluate the safety and efficacy of iclaprim versus vancomycin for treatment of acute bacterial skin and skin-structure infections

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ABSTRACT

Iclaprim, a diaminopyrimidine antimicrobial, was compared with vancomycin for treatment of patients with acute bacterial skin and skin-structure infections (ABSSSIs) in two studies (REVIVE-1 and REVIVE-2). Here, the efficacy and tolerability of iclaprim in a pooled analysis of results from both studies was explored. REVIVE-1 and REVIVE-2 were phase 3, double-blind, randomised, multicentre, active-controlled, non-inferiority (margin of 10%) trials, each designed to enrol 600 patients with ABSSSI using identical study protocols. Iclaprim 80 mg and vancomycin 15 mg/kg were administered intravenously every 12 h for 5–14 days. The primary endpoint was a ≥20% reduction from baseline in lesion size [early clinical response (ECR)] at the early time point (ETP) (48–72 h after starting study drug) in the intent-to-treat population. In REVIVE-1, ECR at the ETP was 80.9% with iclaprim versus 81.0% with vancomycin (treatment difference −0.13%, 95% CI −6.42% to 6.17%). In REVIVE-2, ECR was 78.3% with iclaprim versus 76.7% with vancomycin (treatment difference 1.58%, 95% CI −5.10% to 8.26%). The pooled ECR was 79.6% with iclaprim versus 78.8% with vancomycin (treatment difference 0.75%, 95% CI −3.84 to 5.35%). Iclaprim and vancomycin were comparable for the incidence of mostly mild adverse events, except for a higher incidence of elevated serum creatinine with vancomycin ($n = 7$) compared with iclaprim ($n = 0$). Iclaprim achieved non-inferiority compared with vancomycin for ECR at the ETP and secondary endpoints with a similar safety profile in two phase 3 studies for treatment of ABSSSI suspected or confirmed as caused by Gram-positive pathogens. [Clinical Trials Registration. NCT02600611 and NCT02607618.]

1. Introduction

Up to 1.8% of all hospitalisations are due to acute bacterial skin and skin-structure infections (ABSSSIs) [1]. Often these serious skin infections require intravenous (i.v.) antimicrobials, hospitalisation and/or surgical intervention [2,3]. The majority of ABSSSIs are caused by Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* and

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