Clinical Efficacy of Iclaprim in Complicated Skin and Skin Structure Infection (cSSSI): Results of Combined ASSIST Phase III Studies

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ABSTRACT

Background: The efficacy of iclaprim (ICL) was assessed in two double-blind, placebo-controlled, randomized trials for the treatment of patients with cSSSI. Iclaprim exhibited potent in vitro and in vivo antimicrobial activity against predominant Gram-positive bacteria and was well tolerated in the ASSIST I and II studies. ICL has a differentiated mechanism of action compared with drugs used in this indication and inhibits bacterial dihydrofolate reductase, a critical enzyme in the bacterial folate synthesis pathway. ICL exhibited high eradication rates for all major causative organisms, including methicillin-resistant Staphylococcus aureus. The aim of this study was to evaluate the safety and efficacy of ICL in patients with cSSSI in three combined ASSIST Phase III studies.

Methods: The combination of ASSIST Phase III studies included 440 (ICL) and 445 (placebo) patients randomized to receive ICL or placebo. The treatment was given for 12 hours. The usual dose was 12 mg/kg IV bolus at baseline followed by 6 mg/kg IV q12h for 7 days. The following pathogens were isolated: Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas aeruginosa and Enterococcus faecalis. The Student’s t-test was performed for all data (Arpida AG, Reinach, Switzerland).

Results: The primary endpoint was cure rate at the visit to the site of infection (TOC). Clinical cure was defined as bacterial eradication of the causative pathogens at the TOC visit. The clinical cure rates in the ICL and placebo groups were 87.0% (95% CI = 78.6%–85.5%) and 81.9% (95% CI = 76.4%–70.7%), respectively. The eradication rates for the baseline pathogens were comparable in both treatment groups. The clinical cure rates for the most common isolates were: 92.3% for Staphylococcus aureus, 93.1% for Streptococcus pyogenes, 89.0% for Pseudomonas aeruginosa, and 87.7% for Enterococcus faecalis.

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CONCLUSIONS

The non-inferiority of ICL and ICL compared to placebo was achieved in the ITT, PP and MCE populations, and the percentage of patients who achieved clinical cure was comparable in both treatment groups in all study populations. The eradication of the baseline pathogens was comparable in both treatment groups. The clinical cure rates for the most common pathogen were: 92.3% for Staphylococcus aureus, 93.1% for Streptococcus pyogenes, 89.0% for Pseudomonas aeruginosa, and 87.7% for Enterococcus faecalis.