Friday
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Iclaprim Use Across Various Subpopulations Treated for Bacterial Skin and Skin Structure Infections

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Abstract

Introduction: Patients hospitalized for bacterial skin and skin structure infections are often older, with co-morbid conditions associated with aging such diabetes, obesity, and/or renal impairment. Iclaprim, a dihydrofolate reductase inhibitor, has potent activity against Gram-positive bacteria, including with multidrug resistance. The characteristics of the patient populations exposed to iclaprim in Phase 3 studies were evaluated.

Methods: Baseline characteristics, efficacy and safety were evaluated among patients with skin and skin structure infections. The recent REVIVE-1/-2 studies for acute bacterial skin and skin structure infections (ABSSSI) were randomized, double-blind, multicenter studies of fixed-dose iclaprim 80 mg Q12h compared with vancomycin 15 mg/kg Q12h, both infused over 2h, for 5-14 days. The previous Phase 3 ASSIST-1/-2 studies for complicated skin and skin structure infections (cSSSI) evaluated weight-based iclaprim 0.8 mg/kg Q12h compared with linezolid 600mg Q12h, both infused over 30 minutes, for 10-14 days.

Results: Overall, 1093 patients with cSSSI/ABSSSI have been exposed to iclaprim in the Phase 3 studies with median treatment durations of 7 and 10 days in REVIVE and ASSIST, respectively. 12-15% of the populations were ≥65 years old and BMI up to 65 kg/m2 were treated. Between 9-12% of patients were diabetic and 15-41% had renal impairment. Efficacy and safety were favorable (Table 2, Figure 3).

Conclusions: A broad range of patients with Gram positive cSSSI or ABSSSI, including elderly and/or with co-morbid conditions such as diabetes, obesity, and renal impairment have been treated with iclaprim in the clinical development program.

Introduction

- Patients hospitalized for bacterial skin and skin structure infections are often older, with co-morbid conditions associated with aging such diabetes, obesity, and/or renal impairment.[1,2]
- Iclaprim is a novel diaminopyrimidine antibiotic, which inhibits bacterial dihydrofolate reductase, a critical enzyme in the bacterial folate synthesis pathway.
- Iclaprim has potent activity against Gram-positive bacteria including methicillin-resistant *Staphylococcus aureus*
- Four Phase 3 randomized, double-blind, active-controlled studies have been conducted for the treatment of acute bacterial skin and skin structure infection (ABSSSI).
- The characteristics of the patient populations exposed to iclaprim in these Phase 3 studies were evaluated.

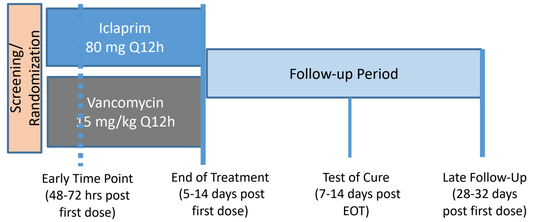
Methods

- Baseline characteristics, efficacy and safety were evaluated among 1,093 patients with skin and skin structure infections in previous Phase 3 studies.

Methods

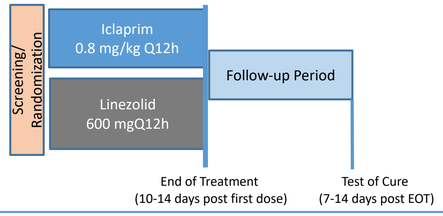
- REVIVE studies for ABSSSI (Figure 1)
  - Randomized (1:1), double-blind, multicenter studies of fixed-dose iclaprim 80 mg Q12h compared with vancomycin 15 mg/kg Q12h, both infused over 2h, for 5-14 days.
  - Primary endpoint: Early clinical response (ECR) defined as ≥20% reduction in lesion size at 48-72 hours after initiating study drug compared with baseline in the ITT population.
  - 10% margin of noninferiority

Figure 1. Study design diagram for the REVIVE-1 and REVIVE-2 studies.



- ASSIST studies for complicated skin and skin structure infections (cSSSI) (Figure 2)
  - Randomized (1:1), double-blind, multicenter studies of weight-based iclaprim 0.8 mg/kg Q12h compared with linezolid 600 mg Q12h, both infused over 30 minutes, for 10-14 days.
  - Primary endpoint: Test of cure response (TOC) defined as clinical cure 7-10 days after end of treatment in the ITT population.
  - 12.5% margin of noninferiority

Figure 2. Study design diagram for the ASSIST-1 and ASSIST-2 studies.



Results

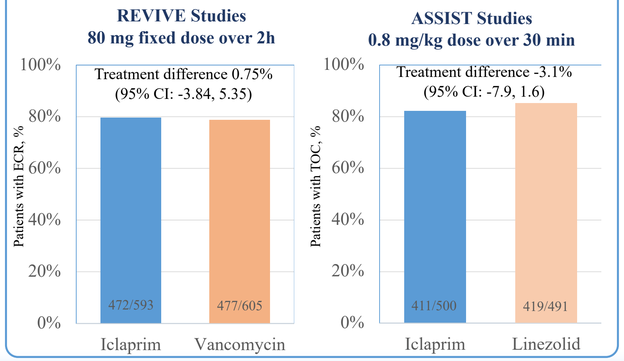
- Overall, 1093 patients with cSSSI/ABSSSI have been exposed to iclaprim in the Phase 3 studies with median treatment durations of 7 and 10 days in REVIVE and ASSIST studies, respectively.
- Demographics and baseline characteristics are shown in Table 1.
  - 12-15% of the populations were ≥65 years old.
  - Comorbidities included diabetes in 9-12% and renal impairment in 15-41% of patients.

Table 1. Demographics and baseline disease characteristics of iclaprim-treated patients in the Phase 3 REVIVE and ASSIST studies.

Baseline Characteristic	REVIVE (n=593)	ASSIST (n=500)
Males, n (%)	381 (64)	322 (64)
Age, years, mean (±SD)	48.2 (14.6)	48.5 (15.2)
White, n (%)	533 (90)	406 (81)
Weight, kg, mean (±SD)	82.3 (20.5)	79.1 (17.0)
Body mass index >35 kg/m²	89 (15)	42 (8)
Injection Drug Use, n (%)	326 (55)	49 (10)
Diabetes, n (%)	56 (9)	61 (12)
Renal impairment (CrCl <90 mL/min), n (%)	90 (15)	206 (41)
Region, n (%)		
United States	419 (71)	195 (39)
Europe	159 (27)	172 (34)
Rest of World	15 (3)	133 (27)

- All 4 Phase 3 REVIVE and ASSIST studies met their primary endpoints (Figure 3).

Figure 3. Early clinical response for the pooled REVIVE studies and test of cure response for the pooled ASSIST studies.



Results

- In general, similar rates of SAEs and discontinuations of study drug due to adverse events occurred within the iclaprim groups compared to the comparators in the overall REVIVE and ASSIST population as well as in relevant subgroups (Table 2).

Table 2. Safety profile of iclaprim in the Phase 3 REVIVE and ASSIST studies.

	REVIVE		ASSIST	
%	Iclaprim	Vancomycin	Iclaprim	Linezolid
Safety Population	n=592	n=599	n=500	N=491
SAEs	4%	5%	4%	3%
DC due to AE	4%	5%	2%	1%
Age ≥65 years	n=73	n=93	n=77	n=62
SAEs	7%	9%	9%	3%
DC due to AE	1%	9%	6%	3%
Diabetes	n=56	n=70	n=61	N=54
SAEs	9%	7%	5%	11%
DC due to AE	4%	10%	5%	4%
Obese (BMI >35 kg/m²)	n=89	n=86	n=42	n=42
SAEs	4%	5%	7%	5%
DC due to AE	6%	6%	2%	2%
Renal Impairment (CrCl <90 ml/min)	n=90	n=124	n=206	N=202
SAEs	7%	5%	3%	3%
DC due to AE	4%	6%	3%	1%

Abbreviations: AE=adverse event, BMI=body mass index, DC=discontinuation, SAEs, serious AEs.

Conclusions

- A broad range of patients (N=1093) with Gram positive cSSSI/ABSSSI, including elderly and/or with co-morbid conditions such as diabetes, obesity, and renal impairment have been treated with favorable efficacy and safety with iclaprim in the clinical development program.
- Fewer discontinuations of iclaprim due to adverse events occurred among the elderly and diabetic patients.

References

1. Miller, et al. *BMC Infect Dis* 2015;15:362.
2. Halilovic, et al. *Journal of Infection* 2012;65:128-134.
3. Huang DB, et al. *Clin Infect Dis* 2018;66:1222-1229.
4. Holland TL, et al. *Antimicrob Agents Chemother* 2018;62:e02580-17.

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