The overall clinical success for all cases with microbiologic confirmation was 69% (42 of 61), indicating that the effectiveness of treatment may be unrelated to the MIC.

The analyses of the pooled SECURE and VITAL data substantiate the view that ISA is effective in the treatment of IA in patients with renal insufficiency, for whom other triazole antifungals may be restricted in use; they also indicate that dose adjustment for this patient population is not needed.

ISA has been approved for use in the United States for treatment of IA and mucormycosis in patients aged 18 years and older. Regulatory review in Europe is ongoing.

Brilacidin: A Novel Antibiotic Designed to Prevent MRSA

Written by Jill Shuman

Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) is a growing problem in the United States and Europe and is a major cause of acute bacterial skin and skin structure infections (ABSSSIs) among otherwise healthy people in the community. Daniel Jorgensen, MD, Cellceutix, Beverly, Massachusetts, USA, presented safety and efficacy data from a phase 2b trial that compared brilacidin (BRI) with daptomycin (DAP) in treating community-acquired ABSSSI caused by *S aureus*.

BRI is a novel synthetic mimic of host defense proteins that has shown in vitro activity against multidrug-resistant *S aureus* in phase 1 and 2a trials. Antibiotics in this category, also known as *defensin mimetics*, kill bacteria in the same manner as the human immune system and thus are less likely to induce antimicrobial resistance. According to Dr Jorgensen, previously presented phase 2a data suggested that BRI was as effective as DAP over 7 days in treating ABSSSI [Jorgensen D et al. ICAAC 2012 (poster L1-1662)]. However, a transient dose-dependent elevation in blood pressure, likely the result of overdosing, was also noted. Therefore, the highest total dose of BRI used in the phase 2b trial (1.2 mg/kg) was less than the lowest total dose (1.6 mg/kg) used in the phase 2a trial.

The phase 2B trial included 215 patients in the United States with an ABSSSI as defined by the FDA [FDA. *Guidance for Industry*. 2013]. Patients were randomized to 1 of 3 BRI injections: low (0.6 mg/kg, single dose), medium (0.8 mg/kg, single dose), or high (0.6 mg/kg on day 1 and 0.3 mg/kg on days 2 and 3). The comparator was DAP (4 mg/kg) for 7 days. The primary end point was early clinical response (48 to 72 hours). Clinical response was defined as a percentage reduction in lesion size ≥ 20% compared to baseline.

Table 1. Clinical Response Rates: All-Treated Population

Study Visit	BRI-SD, Low (n = 53)	BRI-SD, High (n = 53)	BRI-SC, 3 d (n = 53)	DAP, 7 d (n = 50)
48-72 h[a]	45/49 (92.2)	46/48 (95.8)	51/52 (98.1)	45/48 (93.8)
7-8 d[b]	45/49 (91.8)	42/49 (85.7)	48/52 (92.3)	47/50 (94.0)
10-14 d[b]	44/50 (88.0)	39/47 (83.0)	44/47 (93.6)	46/48 (97.9)
21-28 d[b,c]	42/43 (97.7)	39/40 (97.5)	40/42 (95.2)	46/47 (97.9)

Data presented in n/N (%).

BRI, brilacidin; DAP, daptomycin; SC, short course; SD, single dose.

[a]Per FDA definition.

[b]Per investigator.

[c]Sustained clinical response.

The US clinical response rates are shown in Table 1.

According to Dr Jorgensen, there was an early and sustained percentage change in lesion area from baseline to day 7 and again through short-term follow-up (days 10 to 14) in both the all-treated/safety population and the microbiological intent-to-treat population. The most commonly isolated pathogen was *S aureus*, including MRSA. Safety data suggested that patients who received BRI were more likely to experience mild and transient numbness or tingling as compared with the DAP group; however, no increase in hypertension was noted in those randomized to BRI, and no deaths in any group were reported.

In conclusion, Dr Jorgenson emphasized that BRI appears to offer high activity against MRSA. A single dose was safe and effective when compared to a 7-day dose of DAP for the treatment of ABSSSI, which might offer treatment, pharmacoeconomic, and compliance advantages to health care providers and patients.

Macrolides Linked to Cardiac Events in Community-Acquired Pneumonia

Written by Emma Hitt Nichols, PhD

Macrolide antibiotic treatment of community-acquired pneumonia (CAP) was associated with an increased risk of cardiac events, such as arrhythmia and heart failure, compared with other antibiotic therapies. Douwe F. Postma, MD, University Medical Center Utrecht, Utrecht, The Netherlands, presented data from a post hoc analysis of the CAP-START trial [Postma DF et al. *N Engl J Med*. 2015].

International guidelines recommend macrolide antibiotics as treatment of CAP. However, an increased risk of cardiac events has been associated with macrolide