Efficacy and Safety of Sulbactam-Durlobactam (SUL-DUR) Therapy in Patients With *Acinetobacter baumannii-calcoaceticus* Complex (ABC) Infections in the Open-Label Part B of the ATTACK Phase 3 Trial

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Background

- ABC organisms cause severe infections that are difficult to treat due in part to increasing resistance to existing antibacterial therapies
- SUL-DUR is a β-lactam/β-lactamase inhibitor combination in development for treatment of ABC, including carbapenem-resistant and multidrug-resistant (MDR) strains
- The ATTACK Phase 3 trial was a 2-part trial for serious ABC infections

Part A	Part B
Pivotal, randomized, noninferiority SUL-DUR vs colistin (ECCMID 2022 abstract #02060)	Supportive, open-label SUL-DUR treatment Colistin-resistant or intolerant to colistin/polymyxin B

- Here the efficacy and safety of SUL-DUR treatment for patients enrolled in Part B of ATTACK are presented

Part B Methods

N = 28 patients

SUL-DUR (1g/1g) q6h + IMI (1g/1g) q6h × 7–14 days

IMI, imipenem/cilastatin; q6h, every 6 hours.

Endpoints

- **28-day all-cause mortality**
- **Clinical cure[a] at TOC (7 days after end of treatment)**
- **Safety**

[a]Improvement/resolution of symptoms and no additional treatment required.
TOC, test of cure.

- Eligible documented ABC infections included
  - Hospital-acquired bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VABP), ventilated pneumonia
  - Bacteremia (BSI)
  - Complicated urinary tract infections/acute pyelonephritis
  - Surgical or post-traumatic wound infections
- All patients received background therapy of IMI to treat co-infecting non-ABC pathogens

Results – Patient Baseline Characteristics

Table 1. Baseline Characteristics and Demographics (ITT population)	Part B, SUL-DUR (N = 28)
Age, years, n (%)	
Mean ± SD, range	56.2 ± 16.3, 18–80
<65	19 (67.9)
65–75	5 (17.9)
>75	4 (14.3)
Male, n (%)	21 (75.0)
White, n (%)	24 (85.7)
Weight, mean ± SD, kg, range	88.2 ± 24.3, 42–150
Creatinine clearance, mL/min, n (%)	
<90	7 (25.0)
≥90	21 (75.0)
Severity of illness, n (%)	
APACHE II score 10–19/SOFA score 7–9/ qSOFA score 2	19 (67.9)
APACHE II score 20–30/SOFA score ≥10/qSOFA score 3	9 (32.1)
Infection type, n (%)	
BSI	17 (60.7)
HABP	4 (14.3)
VABP	7 (25.0)
Mechanical ventilation, n (%)	8 (28.6)

Table 1. Baseline Characteristics and Demographics (ITT population)	Part B, SUL-DUR (N = 28)
ICU stay, n (%)	
No ICU stay	5 (17.9)
<5 days	1 (3.6)
5–14 days	4 (14.3)
>14 days	18 (64.3)
Polymicrobial infection, n (%) (ECCMID 2022 abstract #02091)	5 (17.9)
Region, n (%)	
Europe	23 (82.1)
Asia-Pacific	4 (14.3)
Latin America	1 (3.6)

- Most patients were male, white, <65 years of age, had CrCL ≥90 mL/min, had bacteremia, had an ICU stay >14 days at baseline
- 16/28 (57.1%) had colistin-resistant infections; 12/28 (42.9%) were intolerant to colistin treatment
- All patients had carbapenem-resistant ABC (CRABC) and MDR infections (ECCMID 2022 abstract #02051)
- Mean ± SD APACHE II score was 18.0 ± 5.0
- 22/28 (78.6%) completed treatment; 3 discontinued treatment due to adverse events, 1 due to death, 1 withdrew consent, and 1 was incorrectly enrolled

CrCL, creatinine clearance; ICU, intensive care unit; SD, standard deviation.

Results – Efficacy

Fig. 1 – All-Cause Mortality Rates (N = 28)

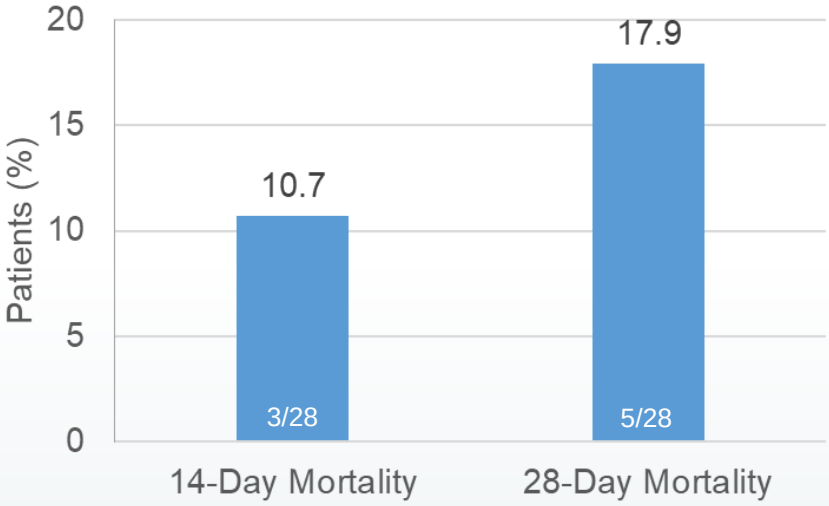
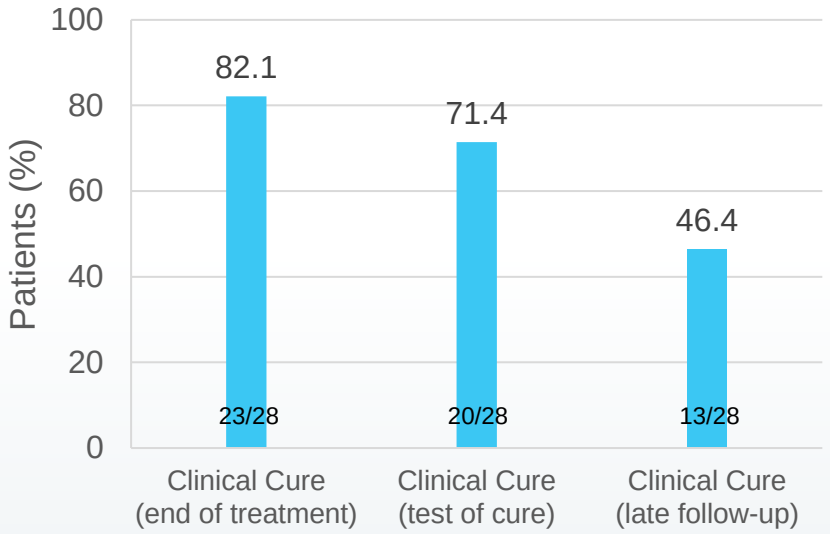


Fig. 2 – Clinical Cure Rates (N = 28)



- The all-cause mortality and clinical cure rates support the efficacy of SUL-DUR treatment including those with ABC bacteremia
- In the subset of 16 patients with colistin-resistant infections, the mortality rate was 18.8% (3/16)
- The ALL-Cause Mortality and Clinical Cure rates in Part B were comparable to the rates observed in Part A of ATTACK (ECCMID 2022 abstract #02060)

Results – Safety

Table 2. Safety Profile of Open-label SUL-DUR Treatment, n (%)	Part B SUL-DUR (N = 28)
Any TEAE	24 (85.7)
Drug-related TEAEs	3 (10.7)
Nausea	1 (3.6)
Neutropenia (serious AE)	1 (3.6)
Proteinuria	1 (3.6)
Increased transaminases	1 (3.6)
TEAEs leading to discontinuation of study drug	4 (14.3)
Abnormal hepatic function	1 (3.6)
Neutropenia	1 (3.6)
Pleural effusion	1 (3.6)
Tic (related to IMI)	1 (3.6)

AE, adverse event; RIFLE, risk, injury, failure, loss, end-stage renal disease; TEAE, treatment-emergent adverse event (patients could have more than 1 TEAE).

- SUL-DUR was well tolerated
- Based on RIFLE criteria, 3/26 (11.5%) had nephrotoxicity (excludes patients on chronic hemodialysis at baseline)
- No clinically significant safety signals emerged due to lab abnormalities, vital signs, and ECGs, other than expected in this critically ill population

Conclusions

- The results of Part B support the efficacy of SUL-DUR treatment in patients that had colistin-resistant ABC, or were intolerant to colistin or polymyxin B therapy including those with bacteremia
- Patients with CRABC infections who were treated with SUL-DUR and IMI had a 28-day mortality rate of 17.9% and a low incidence of drug-related AEs, despite the severity of infections
- These efficacy and safety results are consistent with Part A of the ATTACK trial, and are in contrast with the well-documented AEs associated with last-line therapies for MDR ABC, including colistin
- If approved, SUL-DUR would be an important therapeutic option for ABC infections, including those caused by carbapenem-resistant and MDR strains