Figure 1. Cumulative incidence of premature discontinuation of AFP by D+100

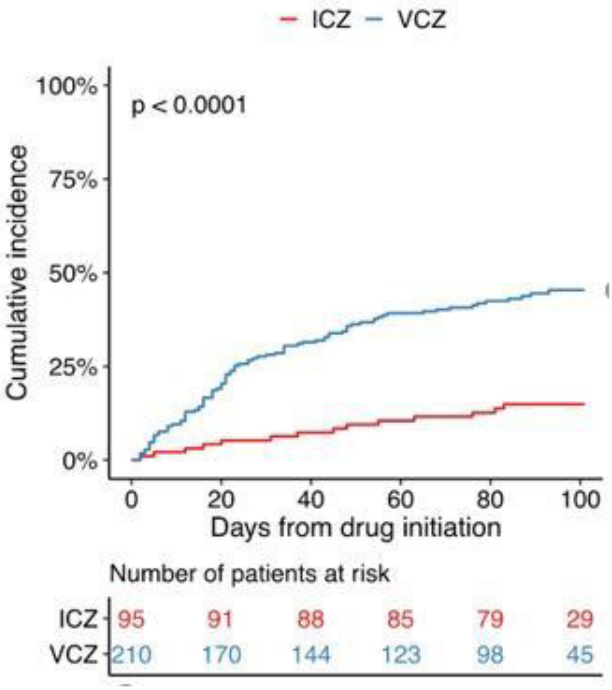


Figure 2. Transaminases at baseline,end of treatment (EOT), EOT +7 days and EOT +14 days in ICZ- and VCZ cohorts

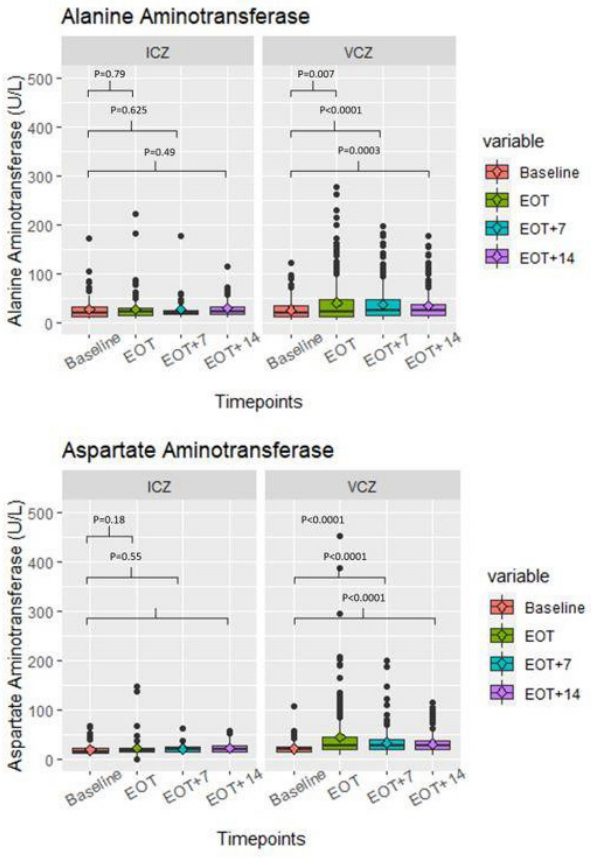
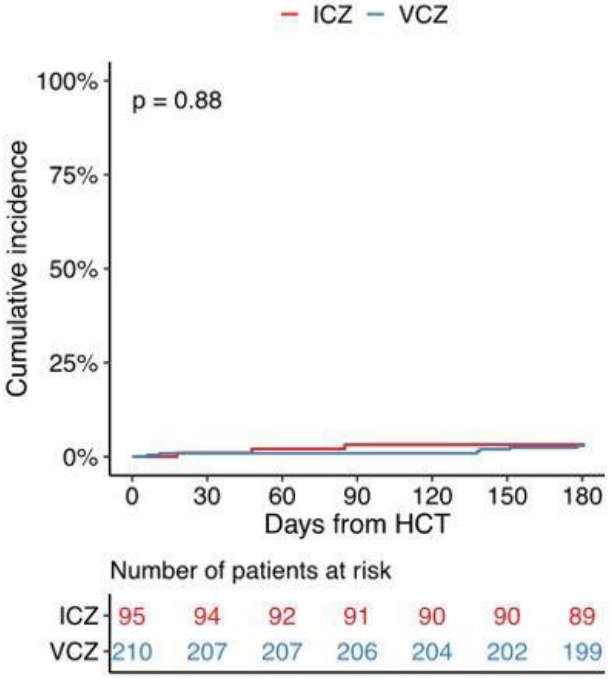


Figure 3. Cumulative incidence of IFI by day +180



Conclusion. There was less premature discontinuation and hepatotoxicity with ICZ AFP, but no increase in IFI or death compared to VCZ AFP in allogeneic HCT pts.

Disclosures. **Yeon Joo Lee, MD, MPH**, **Ansun BioPharma** (Scientific Research Study Investigator)**Astellas Pharma** (Scientific Research Study Investigator) **Sergio Giralt, MD**, **Amgen** (Advisor or Review Panel member, Research Grant or Support, Served an advisory board for Amgen, Actinuum, Celgene, Johnson & Johnson, JAZZ pharmaceutical, Takeda, Novartis, KITE, and Spectrum pharma and has received research support from Amgen, Actinuum, Celgene, Johnson & Johnson, and Miltenyi, Takeda.) **Miguel-Angel Perales, MD**, **Abbvie** (Other Financial or Material Support, Honoraria from Abbvie, Bellicum, Celgene, Bristol-Myers Squibb, Incyte, Merck, Novartis, Nektar Therapeutics, Omeros, and Takeda.)**ASTCT** (Other Financial or Material Support, Volunteer member of the Board of Directors of American Society for Transplantation and Cellular Therapy (ASTCT), Be The Match (National Marrow Donor Program, NMDP), and the CIBMTR Cellular Immunotherapy Data Resource (CIDR) Committee)**Cidara Therapeutics** (Advisor or Review Panel member, Other Financial or Material Support, Serve on DSMBs for Cidara Therapeutics, Servier and Medigene, and the scientific advisory boards of MolMed and NexImmune.)**Kite/Gilead** (Research Grant or Support, Other Financial or Material Support, Received research support for clinical trials from Incyte, Kite/Gilead and Miltenyi Biotec.) **Dionysios Neofytos, MD**, **Basilea** (Advisor or Review Panel member)**Gilead** (Advisor or Review Panel member)**MSD** (Advisor or Review Panel member, Research Grant or Support)**Pfizer** (Advisor or Review Panel member, Research Grant or Support) **Genovefa Papanicolaou, MD**, **Chimerix** (Research Grant or Support)**Merck&Co** (Research Grant or Support, Investigator and received funding and consulting fees from Merck, Chimerix, Shire and Astellas)

1292. Safety Profile of the Novel Siderophore Cephalosporin Cefiderocol in Randomized Phase 2 and Phase 3 Clinical Studies of Serious Gram-Negative Infections

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Session: P-58. Novel Agents

Background. Cefiderocol (CFDC), the first siderophore cephalosporin, is approved in the United States (complicated urinary tract infections [cUTI]) and Europe for the treatment of patients with Gram-negative (GN) infections with limited treatment options.

Methods. This analysis investigated the safety profile of CFDC across three prospective, multicenter, randomized clinical studies: APEKS-cUTI (double-blind, non-inferiority Phase 2 study in patients with cUTI) vs imipenem-cilastatin (1 g/1 g, three-times daily); APEKS-NP (double-blind, non-inferiority Phase 3 study in patients with nosocomial pneumonia [NP]) vs meropenem (2 g, q8h); CREDIBLE-CR (open-label, descriptive Phase 3 study in patients with cUTI, NP, bloodstream infections/sepsis [BSI/sepsis]) caused by carbapenem-resistant GN bacteria; patients in the control arm received best available therapy (BAT; up to 3 agents, dosing based on local label). CFDC was given at 2 g, q8h, infused over 1 (APEKS-cUTI) or 3 (APEKS-NP, CREDIBLE-CR) hours. One adjunctive agent with CFDC was only allowed in CREDIBLE-CR.

Results. 549 patients were treated with CFDC, 347 control treated (Table 1). More than 50% of patients were aged ≥65 years, except BAT arm in CREDIBLE-CR. The majority of patients were admitted to the ICU in APEKS-NP and CREDIBLE-CR. The median treatment duration with CFDC was similar (9–11 days) across studies. The rates of TEAEs and serious AEs (SAEs) between CDFC and comparators were similar in each study (Table 2). The rates of adverse drug reactions were lower with CFDC than with comparators in each study, with a greater difference in CREDIBLE-CR than in APEKS-cUTI and APEKS-NP. TEAEs leading to death rates are shown in Table 2. Eight CFDC-related *Clostridioides difficile* infections occurred across studies (APEKS-cUTI: n=1; APEKS-NP: n=4; CREDIBLE-CR: n=3 [ie, *C. difficile* colitis; pseudomembranous colitis]). In total, eight experienced seizures (APEKS-cUTI: CFDC n=1; APEKS-NP: CFDC n=3, meropenem n=2; CREDIBLE-CR: CFDC n=1, BAT n=1), none of which were related to study drugs. Parameters of iron homeostasis showed no differences between CFDC and comparators.

Table 1. Baseline characteristics and treatment duration (safety populations)

Table 1. Baseline characteristics and treatment duration (safety populations)						
	APEKS-cUTI (NCT02321800)		APEKS-NP (NCT03032380)		CREDIBLE-CR (NCT02714595)	
	Cefiderocol N=300	Imipenem-cilastatin N=148	Cefiderocol N=148	Meropenem N=150	Cefiderocol N=101	BAT N=49
Age						
Mean (SD), years	61.1 (16.5)	61.3 (17.8)	64.7 (14.5)	65.6 (15.1)	63.1 (19.0)	63.0 (16.7)
≥65 years, n (%)	158 (52.7)	78 (52.7)	83 (56.1)	92 (61.3)	64 (63.4)	22 (44.9)
Male, n (%)	137 (45.7)	66 (44.6)	101 (68.2)	104 (69.3)	66 (65.3)	35 (71.4)
ICU, n (%)	NA	NA	103 (69.6)	99 (66.0)	57 (56.4)	21 (42.9)
APACHE II score, mean (SD)	NA	NA	16.1 (6.1)	16.3 (6.9)	15.3 (6.5)	15.4 (6.2)
Severity of diseases						
Mild	33 (11.0)	11 (7.4)	4 (2.7)	7 (4.7)	5 (5.0)	4 (8.2)
Moderate	208 (69.3)	112 (75.7)	73 (49.3)	93 (62.0)	41 (40.6)	22 (44.9)
Severe	59 (19.7)	25 (16.9)	71 (48.0)	50 (33.3)	55 (54.5)	23 (46.9)
Ventilated	NA	NA	91 (62%)	87 (58%)	50 (50%)	26 (53%)
Creatinine clearance						
Mean (SD), mL/min	81.8 (31.6)*	77.6 (32.7)	77.8 (55.1)	82.1 (56.2)	85.8 (79.3)	88.9 (64.2)
Moderate/severe renal impairment,† n (%)	57 (19.0)	35 (23.7)	49 (33.1)	52 (34.7)	43 (42.6)	15 (30.6)
Treatment duration, median (range), days	9 (1–15)	9 (2–15)	10 (2–22)	8.5 (1–22)	NP+B/S: 11 (2–22) cUTI: 10.5 (2–29)	NP+B/S: 13 (2–22) cUTI: 6.5 (2–14)

*N=298. †Moderate 30–50 mL/min; severe <30 mL/min. APACHE II: Acute Physiology And Chronic Health Evaluation II; BAT: best available therapy; B/S: bloodstream infections and sepsis; cUTI: complicated urinary tract infections; ICU: intensive care unit; NA: not available; NP: nosocomial pneumonia; SD: standard deviation

Table 2. Overall safety parameters (safety populations)

Table 2. Overall safety parameters (safety populations)						
	APEKS-cUTI (NCT02321800)		APEKS-NP (NCT03032380)		CREDIBLE-CR (NCT02714595)	
	Cefiderocol N=300	Imipenem-cilastatin N=148	Cefiderocol N=148	Meropenem N=150	Cefiderocol N=101	BAT N=49
TEAEs, n (%)						
Any	122 (40.7)	76 (51.4)	130 (87.8)	129 (86.0)	92 (91.1)	47 (95.9)
Mild	77 (25.7)	36 (24.3)	33 (22.3)	37 (24.7)	23 (22.8)	9 (18.4)
Moderate	39 (13.0)	35 (23.6)	41 (27.7)	47 (31.3)	26 (25.7)	16 (32.7)
Severe	6 (2.0)*	5 (3.4)*	56 (37.8)*	45 (30.0)*	43 (42.6)	22 (44.9)
TEAEs leading to discontinuation	5 (1.7)	3 (2.0)	12 (8.1)	14 (9.3)	10 (9.9)	3 (6.1)
TEAEs leading to death†	1 (0.3)	0	39 (26.4)	35 (23.3)	34 (33.7)	9 (18.4)
Drug-related TEAEs, n (%)						
Any	27 (9.0)	17 (11.5)	14 (9.5)	17 (11.3)	15 (14.9)	11 (22.4)
Drug-related TEAEs leading to treatment discontinuation	3 (1.0)	0 (0)	2 (1.4)	2 (1.3)	3 (3.0)	2 (4.1)
SAEs						
Any	14 (4.7)	12 (8.1)	54 (36.5)	45 (30.0)	50 (49.5)	23 (46.9)
Drug-related	1 (0.3)	1 (0.7)	3 (2.0)	5 (3.3)	1 (1.0)	5 (10.2)

*Adverse events with missing severity were counted as severe. †Death from any cause at the end of study. BAT: best available therapy; TEAEs: treatment-emergent adverse events; SAEs: serious adverse events

Conclusion: CFDC demonstrated a comparable safety profile to carbapenems or other cephalosporins and was generally well tolerated in critically ill patients.

Disclosures. Yuko Matsunaga, MD, Shionogi Inc. (Employee) Takuhiro Sonoyama, MD, Shionogi & Co., Ltd. (Employee) Luis Casanova, PharmD, Shionogi B.V. (Employee) Tsutae Den Nagata, MD, Shionogi & Co., Ltd. (Employee) Roger Echols, MD, Shionogi Inc. (Consultant) Fabio De Gregorio, MD, Shionogi B.V. (Employee) Eriko Ogura, MD, Shionogi & Co., Ltd. (Employee) Simon Portsmouth, MD, Shionogi Inc. (Employee)

1293. Sulbactam-durlobactam is active against recent, multi-drug resistant Acinetobacter baumannii clinical isolates from the Middle East

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Session: P-58. Novel Agents

Background. The incidence of infections caused by multidrug-resistant (MDR) *Acinetobacter baumannii* (*Ab*) is increasing at an alarming rate in certain regions of the world, including the Middle East. Sulbactam (SUL) has intrinsic antibacterial activity against *Ab*; however, the prevalence of β-lactamases in *Ab* has limited its therapeutic utility. Durlobactam (DUR, formerly ETX2514) is a diazabicyclooctenone β-lactamase inhibitor with broad-spectrum activity against Ambler class A, C and D β-lactamases that restores SUL activity *in vitro* against MDR *Ab*. SUL-DUR is an antibiotic designed to treat serious infections caused by *Acinetobacter*, including multidrug-resistant strains, that is currently in Phase 3 clinical development. In global surveillance studies of >3600 isolates from 2012-2017, the MIC_{90} of SUL-DUR was 2 mg/L. Although surveillance systems to monitor MDR infections in the Middle East are currently being established, quantitative, prevalence-based data are not yet available. Therefore, the potency of SUL-DUR was determined against 190 recent, diverse *Ab* clinical isolates from this region.

Methods. 190 *Ab* isolates were collected between 2016 - 2018 from medical centers located in Israel (N = 47), Jordan (N = 36), Qatar (N = 13), Kuwait (N = 42), Lebanon (N = 8), Saudi Arabia (N = 24) and United Arab Emirates (N = 20). Seventy-five percent and 20.5% of these isolates were from respiratory and blood stream infections, respectively. Susceptibility to SUL-DUR and comparator agents was performed according to CLSI guidelines, and data analysis was performed using CLSI and EUCAST breakpoint criteria where available.

Results. This collection of isolates was 86% carbapenem-resistant and 90% sulbactam-resistant (based on a breakpoint of 4 mg/L). The addition of SUL-DUR (fixed at 4 mg/L) decreased the sulbactam MIC_{90} from 64 mg/L to 4 mg/L. Only 3 isolates (1.6%) had SUL-DUR MIC values of > 4 mg/L. This potency was consistent across countries, sources of infection and subsets of resistance phenotypes.

Conclusion. SUL-DUR demonstrated potent antibacterial activity against recent clinical isolates of *Ab* from the Middle East, including MDR isolates. These data support the global development of SUL-DUR for the treatment of MDR *Ab* infections.

Disclosures. Alita Miller, PhD, Entasis Therapeutics (Employee) Sarah McLeod, PhD, Entasis Therapeutics (Employee) Samir Moussa, PhD, Entasis Therapeutics (Employee)

1294. A survey on Vancomycin and Beta Lactams usage in critical care settings in Makkah, Kingdom of Saudi Arabia

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Session: P-59. PK/PD studies

Background. Drug pharmacokinetics/pharmacodynamics (pk/PD) play a vital role in the dose optimization of antimicrobials to maintain targeted effective plasma concentration. Pharmacokinetics parameters e.g., Volume of distribution, clearance, half-life are highly variable in Critically ill patients, therefore require a patient-specific approach to maximize antimicrobials' clinical effectiveness.

The percentage of the dosing interval to ensure free plasma concentration more then MIC is an evidence-based approach to achieve pharmacodynamic targets among critically ill patients. Therefore, using Extended and continuous infusions of Vancomycin and Beta lactams will optimize therapy by promising more time for free plasma concentration above MIC in treatment.

Methods. A self-administered survey was distributed during morning meeting to intensivists to record their attitude and practice towards Vancomycin and Beta lactams usage in intensive care units. The regional institutional review board approved the study of the ministry of health, Makkah, Saudi Arabia.

Results. The response rate was 95 %, as the survey was distributed electronically before the dose optimization workshop conducted at each hospital. The majority (72.5 %) of the intensivists were using only extended infusion for Meropenem in practice. Interestingly, none of the hospitals was familiar with the pk/PD target for vancomycin dosing. Further, most of the intensivists (65 %) were unfamiliar with continuous/extended infusion strategy for Vancomycin in their practice. The majority of them were using traditional trough level target by utilizing standard dosing.

Conclusion. This survey concludes the requirement of a dose optimization policy for beta-lactam and vancomycin in critical settings by utilizing extended/continuous infusion.

Disclosures. **All Authors**: No reported disclosures

1295. Activity of SPR206, a Polymyxin B Derivative, Compared to Colistin Alone and in Combination Against Multidrug-Resistant Pseudomonas aeruginosa Strains

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Session: P-59. PK/PD studies

Background. The emergence of multidrug-resistant (MDR) *Pseudomonas aeruginosa* strains, has resulted in the use of previously discarded antibiotics, such as the polymyxins (polymyxin B and colistin (COL)). Consequently, the polymyxins are continually characterized by the cytotoxicity associated with their use. SPR206 is a polymyxin analogue, however the N-terminal lipophilic side chain has been extensively modified, decreasing the potential for adverse events. SPR206 has reduced minimum inhibitory concentrations (MIC) MIC_{50} and MIC_{90} in *P. aeruginosa* strains when compared to COL. The objective of this study was to compare the *in-vitro* activity of