

the compound, and then observed using time-lapse microscopy revealed that the effect of pravibismine is reversible and that cells recovered 8-12 hrs after removing the compound. Wash out experiments with an *E. coli tolC* strain carrying a plasmid with an IPTG inducible GFP demonstrated that transcription and translation ultimately resumed in most cells after washout. The bioenergetics of the membrane was measured using DiBAC 4(5), a membrane potential sensitive dye which can enter depolarized cells, which revealed that pravibismine caused depolarization of the membrane within 30 mins of exposure in a concentration dependent manner. Finally, a luciferase assay determined pravibismine reduced ATP levels (resulting in decreased luminescence) within 15 mins of exposure in a concentration dependent manner unlike antibiotic controls that had modest or no effect on luminescence.

**Conclusion.** Our results suggest that pravibismine acts rapidly to disrupt cellular bioenergetics, resulting in the immediate cessation of cell growth and protein expression.

**Disclosures.** Brett Baker, M.Sc., D.C., Microbion Corporation (Board Member, Employee)

**1290. Real-World Experience with Omadacycline for Nontuberculous Mycobacterial and Gram-Negative Infections: A Multicenter Evaluation**

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**Session:** P-58. Novel Agents

**Background.** Omadacycline (OMC) is an aminomethylcycline antibiotic in the tetracycline class that has been Food and Drug Administration-approved for acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia. OMC has been shown to have potent *in vitro* activity against a broad-spectrum of Gram-positive and Gram-negative organisms, as well as Nontuberculous Mycobacteria (NTM). Due to its unique activity and availability as an oral agent, off-label use of OMC has been increasing. We evaluated the real-world effectiveness and safety of OMC for a variety of infections.

**Methods.** This was a multicenter, retrospective, observational study that was conducted from January 2020 to June 2020. We included all patients ≥ 18 years of age that received OMC for ≥ 72 hours for any indication and/or pathogen. The primary outcome was clinical success, defined as a lack of 30-day (non-NTM) or 90-day (NTM) mortality or microbiologic recurrence and absence of therapy escalation or alteration. Reasons for OMC utilization and incidence of potential adverse effects attributable to OMC were also analyzed.

**Results.** A total of 18 patients were included from six geographically distinct academic health systems (median age: 56 (IQR, 49-60.5) years; 61% male; 72% Caucasian). The majority of OMC use was in NTM (61%; 100% *Mycobacterium abscessus*) and in *Acinetobacter baumannii* (22%) for bone/joint (39%) and respiratory tract (33%) infections. OMC was used primarily in the outpatient setting alone (83%) and most isolates did not have OMC susceptibility conducted (89%). Clinical success was reported in 83% of the total population (71% non-NTM and 91% NTM). The majority of patients were prescribed OMC due to antimicrobial resistance to previous antibiotic(s) (61%) and/or due to OMC's availability as an oral agent (44%). Three patients experienced side effects while on therapy (serum creatinine elevation, AST/ALT increase, and gastrointestinal distress).

**Conclusion.** OMC appears to be effective and well-tolerated for a variety of infections caused by various pathogens, including *M. abscessus* and *A. baumannii*.

**Disclosures.** Michael J. Rybak, PharmD, MPH, PhD, Paratek (Grant/Research Support)

**1291. Safety of Isavuconazole Compared with Voriconazole as Primary Antifungal Prophylaxis in Allogeneic Hematopoietic Cell Transplant Recipients**

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**Session:** P-58. Novel Agents

**Background.** Voriconazole (VCZ) is used as mold active primary antifungal prophylaxis (AFP) after allogeneic hematopoietic cell transplant (HCT) but is frequently discontinued due to adverse events (AE), variable pharmacokinetics and drug-drug interactions. Limited data exists on the safety of Isavuconazole (ICZ) as AFP in HCT patients (pts). The study objectives were to compare 1) rates of AFP premature discontinuation (d/c), 2) changes in transaminases values from start to end of treatment (EOT) and 3) rates of invasive fungal infections (IFI) and all-cause mortality by Day (D) +180 post HCT between VCZ and ICZ AFP.

**Methods.** This is a matched cohort analysis of 95 pts enrolled in a clinical trial of ICZ AFP from 7/1/2017-10/31/2018 (ICZ-cohort) and 210 pts who received VCZ AFP standard of care between 9/1/2014-12/31/2015 at MSKCC (VCZ-cohort). The cohorts were matched using propensity scores (Table 1). AFP was administered for 75-100 days per institutional guidelines. Premature d/c of AFP was defined as d/c for IFI or AE by D +100 post HCT or interruption of >14 days for any reason. The cumulative incidence function and log rank test were used to compare groups. Mean transaminase values were compared using paired T-tests.

Table 1. Baseline characteristics

Characteristics	Voriconazole (n=210)	Isavuconazole (n=95)	P value
<b>Age (years)</b>			0.180
Median (IQR)	56 (45, 64)	57.4 (50, 66)	
<b>Sex</b>			0.283
Female	82 (39.0%)	31 (32.6%)	
Male	128 (61.0%)	64 (67.4%)	
<b>Disease</b>			0.589
Leukemia	100 (47.6%)	51 (53.7%)	
Lymphoma	42 (20.0%)	16 (16.8%)	
Myelodysplastic syndrome	29 (13.8%)	15 (15.8%)	
Others	39 (18.6%)	13 (13.7%)	
<b>Conditioning Intensity</b>			0.063
Ablative	93 (44.3%)	53 (55.8%)	
Nonablative	117 (55.7%)	42 (44.2%)	
<b>Donor HLA match</b>			0.114
Matched	100 (47.6%)	36 (37.9%)	
Mismatched	110 (52.4%)	59 (62.1%)	
<b>Stem cell source</b>			0.154
Bone marrow	21 (10.0%)	17 (17.9%)	
Cord blood	34 (16.2%)	14 (14.7%)	
Peripheral Blood	155 (73.8%)	64 (67.4%)	
<b>Transplant manipulation</b>			0.446
Ex vivo T cell depletion	78 (37.1%)	31 (32.6%)	
<b>Time to ANC &gt; 500</b>			0.2113
Median (IQR)	12 (11, 15)	12 (11, 18.5)	
<b>Graft vs Host Disease (GvHD)</b>			0.935
GvHD ≥ grade 2	94 (44.7%)	43 (45.2%)	

**Results.** The median (Interquartile range) duration of AFP was 94 (87-100) days and 76 (23-94) days in ICZ and VCZ cohorts respectively (p< 0.0001). Premature d/c occurred in 14/95 (14.7%) of ICZ and 92/210 (43.8%) of VCZ cohorts (p< 0.0001) (Figure 1). The most common cause for AFP d/c was hepatotoxicity: ICZ-cohort: 5/95 (5.26%) vs VCZ-cohort: 48/210 (22.8%). Transaminases at EOT and up to 14 days were increased in VCZ but not ICZ cohort (Figure 2). IFI occurred in 3.15% (3/95) in ICZ-cohort and 2.85% (6/210) in VCZ-cohort (p=0.88) (Figure 3). In ICZ-cohort IFI included 3 *Candida* bloodstream infections (BSI) occurring on ICZ AFP. In VCZ-cohort IFI included one *Candida* BSI after VCZ d/c, and 5 probable mold infections; 3/5 with serum galactomannan > 0.5 and 2 with beta-D-glucan > 80. IFI occurred on VCZ in 1 pt and after VCZ premature d/c in 5 pts. All-cause mortality was 6.31% (6/95) in ICZ-cohort and 2.85% (6/210) in VCZ-cohort (p=0.089).

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

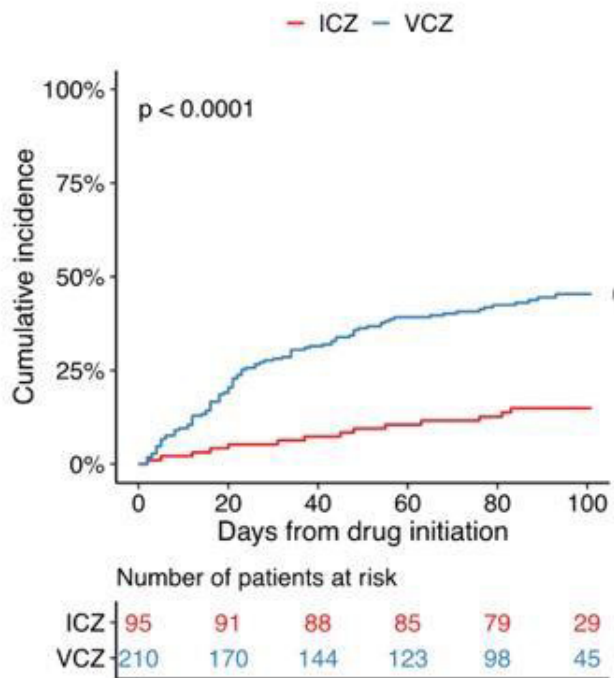


Figure 2. Transaminases at baseline, end of treatment (EOT), EOT +7 days and EOT +14 days in ICZ- and VCZ cohorts

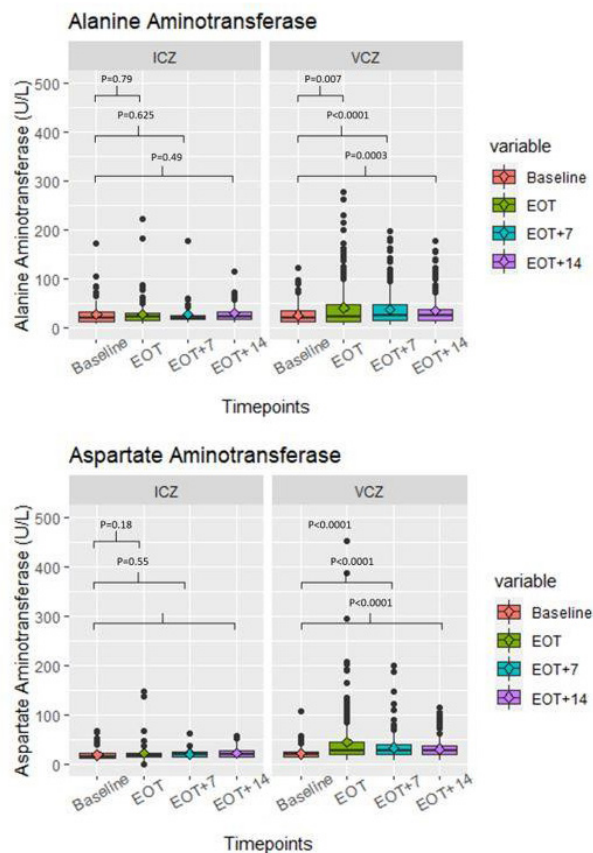
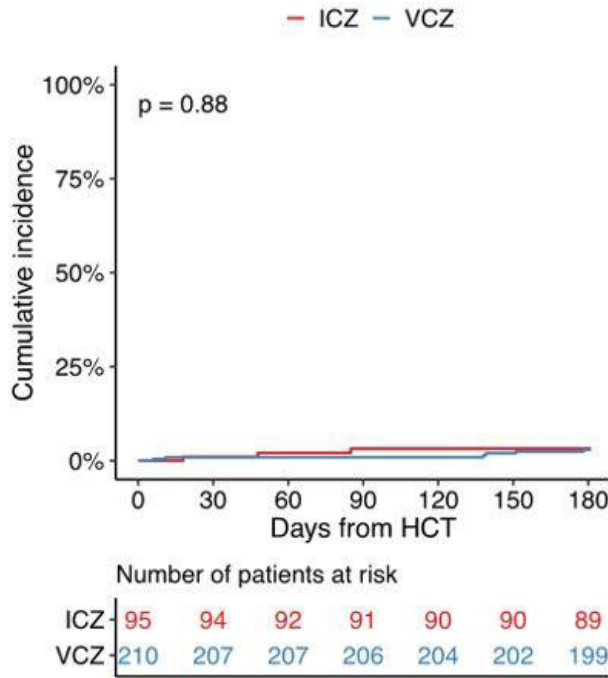


Figure 3. Cumulative incidence of IFI by day +180



**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 Biotech.) 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.