Session: P-49. Infections in Immunocompromised Individuals

Background. Ibrutinib is a tyrosine kinase inhibitor used to treat hematologic malignancies that may increase the risk of serious infection including invasive fungal infections (IFI). In a study of 378 patients with hematologic malignancy on ibrutinib, serious infection and IFI occurred in 11% and 4% respectively (Varughese et al. *Clin Infect Dis*). The primary aims of our study were to determine the incidence of serious infection and associated risk factors in patients on ibrutinib.

Methods. We performed a retrospective analysis of patients with hematologic malignancy prescribed ibrutinib for ≥ 1 week at Yale New Haven Hospital from 2014 to 2019 to identify serious infections defined as those requiring inpatient management. We collected demographic, clinical and oncologic data. Chi-squared tests were used to determine factors associated with an increased risk of infection.

Results. A total of 254 patients received ibrutinib including 156 with CLL, 89 with NHL and 9 with other leukemias. Among these, 21 underwent HSCT, 9 complicated by GVHD. There were 51 (20%) patients with serious infections including 45 (17.7%) bacterial, 9 (3.5%) viral and 5 (2%) IFI (1 pulmonary cryptococcosis, 4 pulmonary aspergillosis). Anti-mold prophylaxis was prescribed to 7 (2.8%) patients, none of whom developed IFI. Risk factors associated with serious infection included ECOG score ≥ 2 (OR 4.6, $p < 0.001$), concurrent steroid use (≥ 10 mg prednisone daily for ≥ 2 weeks; OR 3.0, $p < 0.001$), neutropenia (OR 3.6, $p < 0.01$), lymphopenia (OR 2.4, $p < 0.05$) and maximum ibrutinib dose of 560 mg (OR 2, $p < 0.05$). There was a dose dependent increase in infections based on number of chemotherapy regimens prior to ibrutinib initiation: 14.3% with 0, 19.7% with 1-2 and 28.7% with ≥ 3 prior treatments.

Conclusion. The incidence of serious infection in hematologic patients on ibrutinib was higher than previously reported (20% versus 11%) but the rate of IFI was lower (2% versus 4%). High ECOG score, leukopenia, steroids, and higher ibrutinib doses were associated with an increased risk for serious infection. Targeted antimicrobial prophylaxis should be considered for patients on ibrutinib with these risk factors. Improving functional status may also reduce the risk of infection in patients on ibrutinib.

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

1096. Linezolid versus Tedizolid for the Treatment of Nontuberculous Mycobacteria in Solid Organ Transplant Recipients: An Assessment of Safety

Yi Kee Poon, PharmD[1]; Ricardo M. La Hoz, MD[2]; James Sanders, PharmD[1]; Linda S. Hynan, PhD[1]; Marguerite Monogue, PharmD[1]; [1]University of Texas Southwestern Medical Center, Arlington, Texas; [2]University of Texas Southwestern, Dallas, TX

Session: P-49. Infections in Immunocompromised Individuals

Background. Treatment options for nontuberculous mycobacteria (NTM) infections are limited by the long-term tolerability of antimicrobials. The oxazolidinones, linezolid and tedizolid, display *in vitro* activity against many NTM species and demonstrate excellent oral bioavailability. This study compares the hematologic safety profile of linezolid versus tedizolid for the treatment of NTM in solid organ transplant (SOT) recipients.

Methods. This retrospective cohort study included adult SOT recipients who received linezolid or tedizolid as part of a multi-drug regimen to treat NTM between January 1, 2010 to August 31, 2019. The primary endpoint was the hematologic effects of linezolid versus tedizolid from therapy initiation to week seven. This time frame was chosen based on the median duration of therapy. A mixed-effects ANOVA model was used to assess the effects of linezolid and tedizolid on platelet counts (PLT), absolute neutrophil counts (ANC), and hemoglobin (Hgb) across time. Subjects were treated as a random effect. The secondary analysis described the proportion of adverse effects and discontinuation.

Results. Twenty-four patients were included in the analysis (9 linezolid, 15 tedizolid). *Mycobacterium abscessus abscessus* was the most common isolate, and pulmonary was the most common site of infection (Table 1). The median duration of therapy was 24 days (range 3 to 164 days) and 48 days (range 11 to 571 days) for linezolid and tedizolid, respectively. All patients in the linezolid group received 600 mg daily or less for the majority of treatment duration. In the mixed-effects ANOVA, the ANC decreased in both groups after seven weeks of therapy (p=0.04). Otherwise, no significant effects for week, treatment group, or interaction between week and treatment group were found (Figure 1). Thrombocytopenia and neutropenia were common in both groups, and around one-fifth of patients in each group discontinued the medication due to adverse effects (Table 2).

Table 1. Baseline characteristics of solid organ transplant recipients who received linezolid or tedizolid as part of a multi-drug regimen to treat nontuberculous mycobacteria infections between January 1, 2010 to August 31, 2019 at UT Southwestern Medical Center.

Treatment Group	Linezolid (n = 9)	Tedizolid (n = 15)	p-value
Age, years, median (range)	66 (61-72)	64 (43-71)	0.34
Male, n (%)	8 (89)	9 (60)	0.19
Race, n (%)			0.35
White	8 (89)	10 (67)	
Other	1 (11)	5 (33)	
BMI, median (range)	23 (22-26)	27 (25-30)	0.04
Lung transplant, n (%)	9 (100)	14 (93)	>0.99
Days since transplant, median (range)	361 (27-1041)	200 (0-1343)	0.28
Comorbidities, n (%)			
Cancer	1 (11)	1 (7)	>0.99
CHF	1 (11)	0	0.37
COPD	4 (44)	1 (7)	0.05
CrCl, mL/min, median (range)	67 (49-83)	63 (56-97)	0.90
Cystic fibrosis	0	2 (13.3)	0.51
Diabetes	3 (33)	12 (80)	0.04
ESRD	1 (11)	1 (7)	>0.99
Hypertension	6 (67)	11 (73)	>0.99
Liver disease	0 (0)	1 (7)	>0.99
Stroke	0 (0)	1 (7)	>0.99
Site of Infection, n (%)			-
Bacteremia	1 (11)	4 (27)	
Disseminated	1 (11)	4 (27)	
Osteomyelitis	0	2 (13)	
Pulmonary	7 (78)	12 (80)	
Skin and soft tissue	2 (22)	3 (20)	
Surgical site	0	4 (27)	
Species Isolated, n			-
M. chelonae	1	1	
M. abscessus species	5	4	
M. abscessus abscessus	2	6	
M. abscessus bolleti	2	2	
M. abscessus massilience	0	4	
Baseline platelet count, /μL, median (range)	220 (156-253)	181 (93-304)	0.91
Baseline absolute neutrophil count, /μL, median (range)	5 (3-8)	4 (2-5)	0.36
Baseline hemoglobin, g/dL, median (range)	10 (9-10)	9 (8-10)	0.24
Initial daily linezolid dose, n (%)			-
300 mg	1 (11)	-	
600 mg	3 (33)	-	
1200 mg	5 (56)[a]	-	
Initial daily tedizolid dose, n (%)			-
200 mg	-	14 (93)	
400 mg	-	1 (7)	

[a]Four out of five patients had a dose reduction and the one patient who did not have a dose reduction had 4 days of therapy.

Abbreviations: BMI, body mass index; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; ESRD, end-stage renal disease.

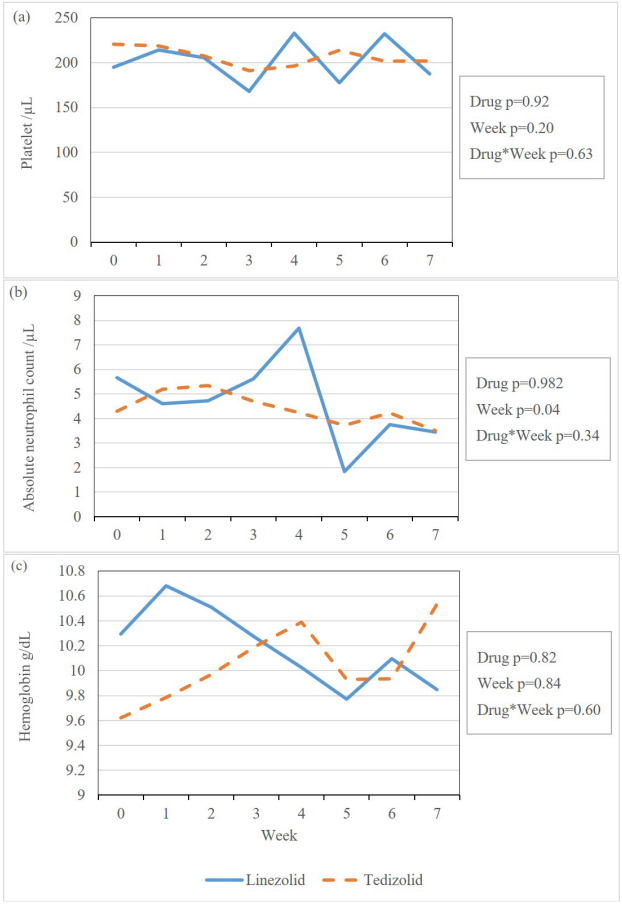
Table 2. Adverse drug events and discontinuation of therapy over seven weeks of therapy.

Treatment Group	Linezolid (n = 9)	Tedizolid (n = 15)
Thrombocytopenia[a]	2 (22)	6 (40)
Criteria 1 (PLT < 150,000 /μL)	2/2 (100)	3/6 (50)
Criteria 2 (PLT > 50% reduction from baseline)	0 (0)	4/6 (67)
Thrombocytopenia, days to onset, median (range)	14 (12-16)	23 (3-37)
Neutropenia[b]	4 (44)	6 (40)
Criteria 1 (ANC < 1500 /μL)	0 (0)	1/6 (17)
Criteria 2 (ANC > 50% reduction from baseline)	4/4 (100)	6/6 (100)
Neutropenia, days to onset, median (range)	21 (2-31)	20 (8-38)
Anemia[c]	1 (11)	0 (0)
Criteria 1 (Hgb <13.5 (male) or 12 (female) g/dL)	1/1 (100)	0 (0)
Criteria 2 (> 30% reduction from baseline)	0 (0)	0 (0)
Anemia, days to onset	6	-
Gastrointestinal effects (nausea and/ or vomiting)[d]	0 (0)	1 (7)
Peripheral neuropathy[d]	0 (0)	0 (0)
Serotonin syndrome[d]	0 (0)	0 (0)
Discontinuation due to ADEs	2 (22)	3 (20)
Discontinuation due to non-ADEs	2 (22)	2 (13)
Deceased	0 (0)	1 (7)
Loss to follow up	1 (11)	0 (0)

[a] Platelet counts < 150,000 /μL or > 50% reduction from baseline
[b] Absolute neutrophil count < 1500 /μL or > 50% reduction from baseline
[c] Hemoglobin <13.5 (male) or 12 (female) g/dL or > 30% reduction from baseline
[d] Based on chart documentations

Abbreviations: ADEs, adverse drug events; ANC, absolute neutrophil count; Hgb, hemoglobin; PLT, platelet.

Figure 1. Effects of linezolid versus tedizolid during the initial seven weeks of therapy using a mixed-effects ANOVA model, (a) platelet counts, (b) absolute neutrophil counts, and (c) hemoglobin.



Conclusion. Non-significant statistical differences were found comparing the effects of linezolid versus tedizolid for PLT, ANC, and Hgb using mixed-effects ANOVA models. Larger cohort studies are required to compare the hematologic adverse effect profile of the oxazolidinones for the treatment of NTM infections in SOT recipients.

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

1097. Microbial Cell Free DNA Sequencing for Prediction of Culture-Negative Infection Events in Children with Cancer

Kathryn Goggin, MD[1]; Amanda griffen, BS[2]; Christina Kohler, BS[2]; Kim J. Allison, RN[2]; Yuki Inaba, BS[3]; Asim A. Ahmed, MD[4]; Desiree D. Hollemon, MSN, MPH[4]; Abigail Brenner, BS[5]; Gabriela Maron, MD[2]; Gabriela Maron, MD[2]; Yilun Sun, MS[2]; Li Tang, PhD[2]; Ellie Margolis, MD PhD[2]; Charles Gawad, MD PhD[6]; Joshua Wolf, MBBS, PhD, FRACP[1]; [1]St. Jude's Children's Research Hospital, Memphis, Tennessee; [2]St. Jude Children's Research Hospital, Memphis, Tennessee; [3]UTSW, Dallas, Texas; [4]Karius, Inc, Redwood City, CA; [5]Indiana University, Indianapolis, Indiana; [6]Stanford University, Stanford, California

Session: P-49. Infections in Immunocompromised Individuals

Background. Culture-independent diagnostics may help diagnose or predict infection; microbial cell free DNA sequencing (mcfDNA-seq), can detect a wide range of pathogens directly from plasma. Immunocompromised children who develop febrile neutropenia (FN) without documented bloodstream infection (BSI) may have undiagnosed bacterial infection, but identification of this is difficult, and the proportion of such episodes is unknown, as is the relative contribution of non-bacterial etiologies. We analyzed mcfDNA-seq results in a convenience sample of FN cases without known etiology.

Methods. Participants were < 25 years of age and undergoing treatment for cancer. Remnant plasma was prospectively obtained and stored. Samples from Days 0 and -1 underwent mcfDNA-seq by Karius Inc., reported in molecules per microliter (MPM) of plasma. Samples from participants without impending or recent fever or infection were also tested.

Results. There were 8 episodes in 7 patients; 4 (50%) had a common bacterial pathogen identified by mcfDNA-seq on Day 0 (**Table 1**). In 2 (50%) of these cases, the same organism was also identified on Day -1, at a lower concentration. One fungal pathogen was identified prior to and at onset of FN. A common bacterial pathogen was identified in 3/64 (5%) control samples from the population.

Culture-negative sepsis was the final diagnosis in one episode; *Streptococcus mitis*, an important cause of neutropenic sepsis, was found in Day 0 and Day -1 samples. In an episode where *E. coli* was identified by mcfDNA-seq, FN recurred after antibiotic discontinuation.

Table 1. Quantitative mcfDNA-seq Results for Prediction & Diagnosis of Febrile Neutropenia Episodes

Table:

Quantitative mcfDNA-seq Results for Prediction & Diagnosis of Febrile Neutropenia Episodes

		Common Bacterial Pathogens (Organism, MPM)		Other Organisms (Organism, MPM)	
Episode	HCT	Day 0	Day -1	Day 0	Day -1
1	Yes	*Streptococcus mitis*, 657	*S. mitis*, 379	None	None
2	No	*Escherichia coli*, 5728	*E. coli*, 98	None	*Helicobacter pylori*, 49
3	Yes	*S. mitis*, 206	None	*Mucor velutinosus*, 559	*M. velutinosus*, 382 HHV5 (CMV), 27
4	No	*Streptococcus oralis*, 257 *Streptococcus sanguinis*, 131 *Fusobacterium nucleatum*, 708	*Staphylococcus epidermidis*, 113	*Tannerella forsythia*, 136 *Rothia dentocariosa*, 118 *Propionibacterium propionicum*, 131 *Cardiobacterium hominis*, 89 *Prevotella loescheii*, 119 *Gemella morbillorum*, 43 *Campylobacter gracilis*, 49 *Corynebacterium matruchotii*, 431 *Actinomyces oris*, 251 *Campylobacter concisus*, 34 *Neisseria mucosa*, 271 *Actinomyces viscosus*, 750 *Parvimonas micra*, 28 *Campylobacter showae*, 102 *Neisseria elongate*, 112 *Prevotella melaninogenica*, 49 *Neisseria flavescens*, 331 *Veillonella parvula*, 158 *Capnocytophaga granulosa*, 238	*Staphylococcus saprophyticus*, 29 *Prevotella melaninogenica*, 26 *Staphylococcus capitis*, 72
5	Yes	None	None	None	None
6	Yes	None	None	HHV5 (CMV), 68	HHV5 (CMV), 92
7	Yes	None	None	*Bacteroides ovatus*, 21 *Bacteroides vulgatus*, 31	*B. ovatus*, 91
8	No	None	None	*Bacteroides thetaiotaomicron*, 56	*B. thetaiotaomicron*, 34

MPM, concentration of pathogen cell free DNA in molecules per microliter of plasma; HCT, History of allogeneic hematopoietic cell transplantation

Conclusion. In this sample of culture-negative FN episodes in pediatric patients leukemia, mcfDNA-seq identified a bacterial pathogen in 50% of cases. The same organism was identifiable on the day prior to FN in 50% of cases, suggesting that predictive testing might be feasible.

Disclosures. Asim A. Ahmed, MD, Karius (Employee) Desiree D. Hollemon, MSN, MPH, Karius inc (Employee) Charles Gawad, MD PhD, Karius inc (Grant/Research Support) Joshua Wolf, MBBS, PhD, FRACP, Karius inc (Grant/Research Support)

1098. Norovirus Infection in Cancer Patients Undergoing Chimeric Antigen Receptor T-cell Immunotherapy (CAR-T)

Divya S. Kondapi, MD[1]; Sasirekha Ramani, PhD[2]; Adilene Olvera, MPH MLS (ASCP)[3]; Robert L. Atmar, MD[2]; Mary K. Estes, PhD[2]; Pablo C. Okhuysen, MD, FACP, FIDSA[3]; [1]1. Section of Infectious Diseases, Baylor College of Medicine 2.Department of Infectious Diseases,The University of Texas,MD Anderson Cancer Center, houston, Texas; [2]Baylor College of Medicine, Houston, TX; [3]The University of Texas MD Anderson Cancer Center, Houston, Texas, Houston, TX

Session: P-49. Infections in Immunocompromised Individuals

Background. CAR-T is used to treat certain refractory hematological malignancies. B-cell aplasia and immunosuppression used to treat CAR-T side effects increase infection risk. Little data are available describing Norovirus (NoV) infections in CAR-T recipients.

Methods. We reviewed the medical records of 134 patients with NoV diarrhea (identified by nucleic acid amplification test) between 2016-2019. Of these patients, nine received CAR-T prior to developing NoV. Here we describe their demographics, clinical characteristics, treatments, and complications.

Results. The median age was 49 years (Table 1). Patients' underlying malignancies included Non-Hodgkin's Lymphoma (4), Acute Lymphoblastic Leukemia (3), Chronic Lymphocytic Leukemia (1) and metastatic Sarcoma (1). Prior to development of NoV, six patients had undergone hematopoietic stem cell transplant, and 1 had received checkpoint inhibitor therapy. Five patients experienced cytokine release syndrome after CAR-T, and 1 experienced CAR-T-related encephalopathy syndrome (Table 2). Two patients received interleukin-6 antagonist therapy, and one received high dose steroids. Time to diarrhea onset post-CAR-T cell infusion was variable(median 256days, IQR 26-523 days).Six had an absolute lymphocyte count< 1000/mm3 at diarrhea onset. Three had diarrhea for >14 days; median diarrhea duration in the other 6 patients was 4 days. Other GI complaints included abdominal pain (3), nausea (4), and vomiting (3). For NoV treatment, three received oral immunoglobulin, and 8 received Nitazoxanide. Complications included development of concomitant GI-GVHD(5), ileus (2), need for TPN (3), renal failure requiring dialysis (2), ICU stay (3), and death (2). Two patients were co-infected with other enteropathogens such as rotavirus, enteropathogenic and enteroaggregative *E.Coli* and *Clostridioides difficile*. Three patients with diarrhea lasting >14 days had serial samples collected over time; NoV shedding lasted 81-546 days. NoV was genotyped in 6 patients(Table 3) and included GII.2(2), GII.4(2), GII.6(1) and GII.12(1).