Background. Lymphodepletion chemotherapy followed by CD19-targeted chimeric antigen receptor-modified T (CAR-T) cell infusion is a novel treatment for refractory B cell malignancies. Infectious complications of CD19 CAR-T cell immunotherapy have not been studied.

Methods. We described infections between 0–28 and 29–90 days after CD19 CAR-T cell infusion in patients with relapsed and/or refractory CD19+ malignancies treated in a phase 1/2 open-label trial (NCT01865617). We used Poisson and Cox regression to evaluate pre- and post-CAR-T cell infusion risk factors for infection, respectively. Patients receiving anti-tumor therapy after CAR-T cell infusion were censored.

Results. The cohort included 133 patients with acute lymphoblastic leukemia (ALL, n = 47), chronic lymphocytic leukemia (CLL, n = 24), and non-Hodgkin lymphoma (NHL, n = 62). There were 43 infections in 30 patients (22.6%) within 28 days after CAR-T cell infusion with a mean of 1.19 infections per 100 days-at-risk (Fig 1). Among 119 patients followed at our center from day 29–90, there were a mean of 0.67 infections per 100 days-at-risk. Six patients (4.5%) developed invasive fungal infections. Infection was a primary or secondary cause of death in 2 patients (1.5%). Pre-CAR-T cell infusion factors that were associated with more infections included a diagnosis of ALL, >=4 prior chemotherapeutic regimens, and highest CAR-T cell dose (2×10^7 cells/kg) (p values <0.001). After CAR-T cell infusion, severe (grade 4–5) cytokine release syndrome (CRS) was associated with a >3-fold increased hazard for infection ($P < 0.001$) and was the primary risk factor. Patients receiving an optimized lymphodepletion and CAR-T cell dose regimen had a mean of 0.74 and 0.63 infections per 100 days-at-risk between days 0–28 and 29–90 with no fatal infections.

Conclusion. The incidence of infectious complications after CD19 CAR-T cell immunotherapy was similar to that seen in patients with relapsed and/or refractory B cell malignancies receiving salvage chemoimmunotherapies. Patients with more prior chemotherapy regimens and severe CRS after CAR-T cell infusion had the highest risk for infection. Fatal infections were rare, and patients receiving optimized regimens had fewer infectious complications.

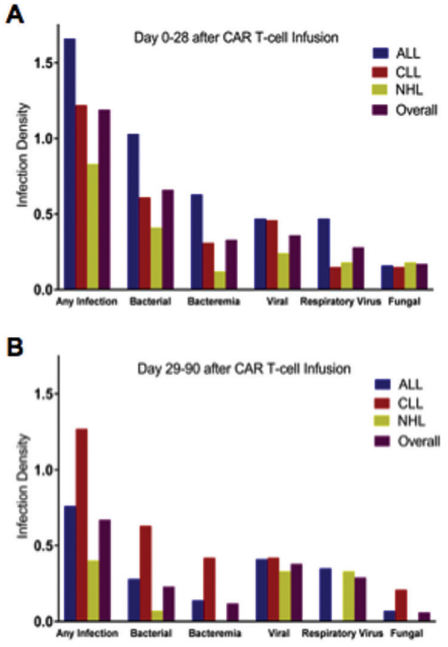

Figure 1. Infection densities for any and specific infection categories after CAR-T cell infusion
To account for multiple infections per patient, we calculated the infection density, or mean number of infections per 100 patient days-at-risk, by dividing the number of infections per patient by the number of days-at-risk and normalizing over 100 days. We calculated this value for infections occurring during A) the first 28 days and B) day 29 to day 90 after CAR-T cell infusion. Bacteremia and respiratory virus categories are subsets of the bacterial and viral categories, respectively.

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2350. Opportunistic Infections (OIs) in Patients with Hematologic Malignancies (HM) Treated with Bruton's Tyrosine Kinase (BTK) and Phosphoinositide 3 Kinase (PI3K) Inhibitors: An 8-Year Retrospective Cohort Study

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Background. BTK and PI3K inhibitors are increasingly used for treatment in patients with HM. OIs when these agents were used as first line therapy signaled an increased level of immunosuppression beyond what was expected from the mechanism of action of these drugs. The epidemiology of OIs in the setting of BTK and PI3K inhibitor use has not been characterized.

Methods. We retrospectively studied a cohort of patients with HM who received BTK (ibrutinib, acalabrutinib, spebrutinib) or PI3K (idelalisib, duvelisib, TGR-1202) inhibitors as part of clinical trials at our center between March 2008 and November 2016. Patients were followed up until April 30, 2017. Incident infectious complications were recorded. Cohort baseline characteristics, underlying malignancy, stage of disease, type of therapy and use of antimicrobial prophylaxis were recorded.

Results. 148 patients who received BTK or PI3K inhibitors as first or second line therapy were included in the study. Median age was 64.5 years, 32% were female, 95.9% had chronic lymphocytic leukemia (CLL), 4.1 % had Non-Hodgkin Lymphoma (NHL). Sixty-three percent received BTK inhibitors and 37% received PI3K inhibitors as first line therapy. Pneumocystis and HSV/VZV prophylaxis were used in 82.4% and 85.8% of patients, respectively. Twenty-seven OIs occurred in 24 patients. The most common OIs were pneumocystosis (7), aspergillosis (5) HSV (3), VZV (3), CMV (2), Cryptococcal meningitis (2), candidiasis (2) and other invasive mold infections (3). Seventy-one patients (48%) had infectious episodes not considered OIs. Median time to onset of OIs after start of therapy was 78 days (range, 6–323). Twelve OIs (8.1 %) occurred after first line therapy with BTK inhibitors, 11 OIs (7.4 %) occurred after first line PI3K inhibitors.

Conclusion. The use of BTK and PI3K inhibitors as first or second line treatment of CLL or NHL are associated with incident OIs. Clinical awareness of these complications and the use of adequate prophylactic and/or monitoring strategies are essential in preventing serious OIs in this population.

Disclosures. **J. Brown**, Pharmacyclics, Janssen, Celgene, Gilead, Infinity, Genentech, and Pfizer, Roche and Sun BioPharma, Janssen, Gilead, Sun BioPharma, and Pfizer: Consultant, Consulting fee; **F. Marty**, Astellas Pharma US: Consultant and Grant Investigator, Consulting fee and Grant recipient; Chimerix: Consultant and Grant Investigator, Consulting fee and Grant recipient; Fate Therapeutics: Scientific Advisor, Consulting fee; Gilead Sciences: Consultant and Grant Investigator, Consulting fee and Grant recipient; LFB: Consultant, Consulting fee; Merck: Consultant, Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient; Roche Molecular Systems: Consultant, Consulting fee; Shire: Consultant and Grant Investigator, Consulting fee and Grant recipient

2351. Change in Clinical Management Associated with Flexible Bronchoscopy and Bronchoalveolar Lavage in Hematopoietic Stem Cell Transplant Recipients with New Pulmonary Infiltrates

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Background. Pulmonary complications occur in 60% of hematopoietic stem cell transplant (HSCT) recipients with significant morbidity and mortality. Bronchoscopy with bronchoalveolar lavage (BAL) is an important diagnostic tool, but yield can be variable. The aim of this study was to investigate the utility of BAL in HSCT patients with new pulmonary infiltrates and determine factors associated with higher BAL yield.

Methods. Retrospective review of BAL results from January 2014 to July 2016. Included first bronchoscopy for HSCT patients over 18 years of age. Positive BAL determined by positive culture (bacterial, fungal, mycobacteria), viral PCR, elevated *aspergillus* galactomannan antigen (AGA), and cytology. Logistic regression analysis was performed.

Results. 54 HSCT recipients were included: 93% allogeneic, 34% neutropenic, 39% on prednisone, 59% on supplemental oxygen, 8% receiving mechanical ventilation (MV), 85% with multilobar infiltrates, 92% on antimicrobials (antibacterial 83%, antifungal 92%, antiviral 13%). 65% had positive BAL (23/54 bacterial, 16/54 elevated AGA, 6/54 fungal, 14/54 viral PCR, 1/54 mycobacteria). Median time to BAL from HSCT was 7.5 months. Not on levofloxacin prophylaxis ($P = 0.004$), not on MV ($P = 0.037$), or unrelated donor were associated with positive BAL results. Positive bacterial BAL culture was predictive of antibacterial escalation ($P < 0.001$). Elevated BAL AGA was associated with antifungal escalation and antibacterial de-escalation ($P = 0.012$). Antiviral initiation was more likely with positive BAL PCR ($P = 0.002$). Antifungal de-escalation ($P = 0.047$) and steroid initiation ($P = 0.010$) were more likely with negative BAL. 6 month mortality was 41%, and more likely with positive bacterial BAL culture ($P = 0.046$). Overall positive BAL was not predictive of mortality.

Conclusion. Bronchoscopy with BAL assisted in making critical management changes: elevated AGA with antifungal escalation and antibacterial de-escalation; and negative BAL with prednisone initiation and antifungal de-escalation. Unrelated donors, patients not on levofloxacin, or not on MV were more likely to have a positive BAL. Antimicrobial use likely reduced diagnostic yield for bacterial pathogens. Overall 6 month mortality was high, especially among those with bacterial infections.

Characteristic	OR Positive BAL (95 %CI)	P
Overall change in management		
Escalation of antibiotics	2.96 (0.88, 10.01)	0.091
De-escalation of antibiotics	1.44 (0.46, 4.53)	0.577
Escalation Antifungals	2.96 (0.88, 10.01)	0.091
De-escalation antifungals	0.11 (0.01, 1.07)	**0.047**
Escalate steroids	0.13 (0.03, 0.57)	**0.010**
Outcome		
Readmission within 1 months	1.30 (0.34, 4.94)	1.000
Repeat bronchoscopy in 3 months	0.75 (0.22, 2.56)	0.753
6-month mortality	3.30 (0.80, 13.58)	0.123

Factor	OR Positive BAL (95 %CI)	P
Female	10.23 (1.68, 97.76)	**0.010**
Related	0.09 (0.010, 0.58)	**0.046**
Neutrophils <1000	0.50 (0.08, 3.03)	0.448
Days admitted prior to BAL	0.98 (0.92, 1.04)	0.485
Mechanical ventilation	0.04 (<0.01, 0.82)	**0.037**
Oxygen requirement	4.90 (0.94, 33.17)	0.059
Prednisone	4.72 (0.93, 33.64)	0.062
Levofloxacin prophylaxis	0.08 (0.01, 0.48)	**0.004**
Antifungal prophylaxis	0.65 (0.09, 4.17)	0.653

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2352. Prediction of Febrile Neutropenia after Chemotherapy Based on Pretreatment Risk Factors among Cancer Patients

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Background. Febrile neutropenia (FN) is a common complication to chemotherapy associated with a high burden of morbidity and mortality. Reliable prediction of individual risk based on pretreatment risk factors allows for stratification of preventive interventions. We aimed to develop such a risk stratification model to predict FN in the 30 days after initiation of chemotherapy.

Methods. We included consecutive treatment-naïve patients with solid cancers and diffuse large B-cell lymphomas at Copenhagen University Hospital, 2010–2015. Data were obtained from the PERSIMUNE repository of electronic health records. FN was defined as neutrophils ≤0.5 × 10E9/L at the time of either a blood culture sample or death. Time from initiation of chemotherapy to FN was analyzed using Fine-Gray models with death as a competing event. Risk factors investigated were: age, sex, body surface area, haemoglobin, albumin, neutrophil-to-lymphocyte ratio, Charlson Comorbidity Index (CCI) and chemotherapy drugs. Parameter estimates were scaled and summed to create the risk score. The scores were grouped into four: low, intermediate, high and very high risk.

Results. Among 8,585 patients, 467 experienced FN, incidence rate/30 person-days 0.05 (95% CI, 0.05–0.06). Age (1 point if > 65 years), albumin (1 point if < 39 g/L), CCI (1 point if > 2) and chemotherapy (range -5 to 6 points/drug) predicted FN. Median score at inclusion was 2 points (range –5 to 9). The cumulative incidence and the incidence rates and hazard ratios of FN are shown in Figure 1 and Table 1, respectively.

Conclusion. We developed a risk score to predict FN the first month after initiation of chemotherapy. The score is easy to use and provides good differentiation of risk groups; the score needs independent validation before routine use.

Table 1. Incidence rates and hazard ratios of developing FN

Risk group	N (%)	Risk score	Incidence rate/30 person-days (95% CI)	Hazard ratio (95% CI)
Low	4,859 (57)	<3	0.02 (0.02-0.02)	Reference
Intermediate	1,881 (22)	3-4	0.07 (0.06-0.08)	3.4 (2.6-4.4)
High	1,747 (20)	5-7	0.14 (0.13-0.16)	7.2 (5.7-9.2)
Very high	98 (1)	8+	0.31 (0.21-0.45)	15.5 (9.9-24.3)

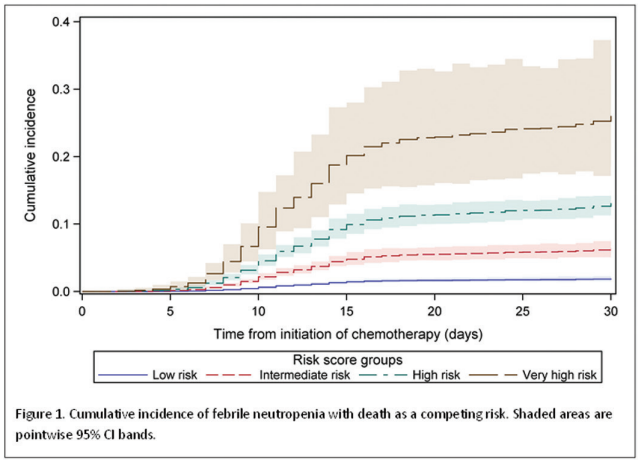

Figure 1. Cumulative incidence of febrile neutropenia with death as a competing risk. Shaded areas are pointwise 95% CI bands.

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

2353. Infections in Patients Receiving Ibrutinib for Treatment of Lymphoma: A Single-center Experience

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Background. Ibrutinib is an inhibitor of Bruton's tyrosine kinase (BTK), a key kinase in the B-cell receptor pathway that plays a significant role in the survival of B-cells. Ibrutinib has been approved for the treatment of several B-cell malignancies. Recently, a few cases of opportunistic infection in patients receiving Ibrutinib therapy have been reported. We aimed to determine the scope of infection in patients with lymphoid malignancies who received treatment with Ibrutinib.

Methods. Retrospective review of patients with lymphoid malignancies who received at least 30 consecutive days of Ibrutinib (monotherapy or combination) from December 2012–December 31, 2016. Infections were defined based on Infectious Diseases Society of America (IDSA) criteria and revised 2008 European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group (EORTC) guidelines. Charts reviewed for a minimum of 6 months to determine development of infection.

Results. Charts of 250 patients who received treatment with Ibrutinib were reviewed. Thirty-six excluded as they were lost to follow-up or received less than 30 days of Ibrutinib therapy. Among the 214 patients included, mean age was 65 (range 31–92) years and 161 (75%) were men. Eleven patients (5.1%) developed infection during the follow-up period: six cases of invasive aspergillosis (IA) (six pulmonary and one also involved the central nervous system (CNS)), twp cases of methicillin-resistant *Staphylococcus aureus* pneumonia, one case of CNS cryptococcal meningitis, one PJP Pneumonia, and one disseminated zoster (CNS meningoencephalitis). Of the 11 patients who developed infection, none was neutropenic at the time of infection and none received substantial corticosteroid courses. Apart from one patient who received combination therapy with ofatumumab, all patients who developed infection were receiving Ibrutinib monotherapy prior to the onset of infection.

Conclusion. Our data demonstrate that patients receiving Ibrutinib therapy for lymphoid malignancies are at risk for serious infections, including invasive fungal infections. The majority of infections in these patients developed in the absence of other risk factors for infection, suggesting that Ibrutinib may be independently associated with increased risk for certain infections.