578. Infections in Patients Treated with Chimeric Antigen Receptor T-cells (CAR-T) therapy
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Session: P-22. Care Strategies for Transplant Patients
Background: Although chimeric antigen receptor T cells (CAR-T) therapy is a promising novel therapy for the treatment of relapsed or refractory (R/R) B-cell malignancies, data on infectious complications associated with this therapy are limited. Therefore, further assessment of infections following CAR-T therapy is warranted.
Methods: We retrospectively reviewed and analyzed infectious complications within 6 months following CAR-T therapy infusion (CTI) in 39 adult and pediatric patients with R/R acute lymphoblastic leukemia (ALL) and Non-Hodgkin Lymphoma (NHL) at Michigan Medicine.
Results: Overall, 20 infections were identified in 16 of 39 patients (41%) following CTI (Table 1). The majority of infections were caused by various bacteria or respiratory viruses in a cohort of patients with lymphoma as the most common underlying malignancy.
Conclusion: Infections complications are common following CAR-T therapy. We found the majority of infections to be caused by various bacteria or respiratory viruses in a cohort of patients with lymphoma as the most common underlying malignancy.

579. Prophylactic Antibiotics Did Not Decrease Recurrent Cholangitis in Patients with Biliary Atresia After Kasai Portenterostomy
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Session: P-22. Care Strategies for Transplant Patients
Background: Biliary atresia (BA) is a rare, progressive, idiopathic, fibro-obliterative disease of the extrahepatic biliary tree seen in children. The current standard treatment is surgical management with Kasai portenterostomy (KP). Bacterial cholangitis is a frequent complication following KP and an important determinant of long-term prognosis. Use of prophylactic antibiotics is common but not universal and efficacy is controversial.
Methods: A retrospective study was performed that included all patients with BA who underwent KP from November 2002 to July 2019. Chart review was conducted to collect demographic information and evaluate the use of antibiotic prophylaxis, number of cholangitis episodes, time to liver transplantation (LTV), and survival.
Results: Ninety-one patients with BA underwent KP during the study period. Seventy-two (79%) received prophylactic antibiotics, and 19 (21%) did not. The median duration of prophylactic antibiotics was 7 months (interquartile range [IQR] 8.5). Patients in the no-prophylaxis group had significantly fewer cholangitis episodes (median 0, IQR 1) than in the antibiotic prophylaxis group (median 1, IQR 2); p = 0.02. The median time to LTV was 8 months (IQR 8.5) in the antibiotic prophylaxis group, compared to 7 months (IQR 6) in the no-prophylaxis group, p = 0.88. Of the patients who were on antibiotic prophylaxis, 57 (79.2%) received trimethoprim-sulfamethoxazole (TMP-SMX) alone and 15 (20.8%) received multiple/other antibiotics. Seventy patients (7.7%) had culture-positive cholangitis. Six of 7 received prophylaxis with TMP-SMX and 5 of 7 grew bacteria that were resistant to TMP-SMX. No deaths occurred between the postoperative KP period to the time of LTV in both groups.
Conclusion: Prophylactic antibiotics did not decrease recurrent cholangitis in patients with BA after Kasai portenterostomy. Further assessment of infections after CAR-T therapy is warranted.

Table 1. Comparison of early vs late infection after CAR-T Infusion

| Characteristic | All Infections (%) | Early (0-30 Days) (%) | Late (31-180 Days) (%) | P-value |
|---------------|-------------------|----------------------|------------------------|---------|
| Any infection | 20 (41)           | 6 (20)               | 14 (47)                | 0.018   |
| Bacterial infection | 8 (40) | 6 (20) | 2 (12) | 0.020 |
| Bacteremia | 4 (20)           | 2 (10)               | 2 (10)                 |         |
| SSI1 | 1 (5)            | 1 (5)                | 0 (0)                  |         |
| UTI2 | 2 (10)           | 2 (10)               | 0 (0)                  |         |
| CDI | 1 (5)            | 1 (5)                | 0 (0)                  |         |
| Fungal infection | 2 (10) | 0 (0) | 2 (10) | 0.495 |
| FUNG1 | 1 (5) | 1 (5) | 0 (0) |         |
| SSI (Aspergilus and Rhizopus) | 1 (5) | 1 (5) | 0 (0) |         |
| Viral infection | 10 (50) | 2 (10) | 8 (40) | 0.062 |
| CMV | 2 (10)           | 1 (5)                | 1 (5)                  |         |
| HSV | 2 (10)           | 2 (10)               | 0 (0)                  |         |
| Rhinovirus Enterovirus | 2 (10) | 2 (10) | 0 (0) |         |
| Parainfluenza | 2 (10) | 1 (5) | 1 (5) |         |
| Metapneumovirus | 1 (5) | 1 (5) | 0 (0) |         |

Overall, 20 infections were identified in 16 patients (41%). SSI, skin and soft tissue infection; UTI, urinary tract infection; CDI, Clostridium difficile infection; CMV, cytomegalovirus; RSV, respiratory syncytial virus.

Table 2. Demographic, Laboratory, and Clinical Characteristics

| Characteristic | All Patients (n=91) | Infected Patients (n=20) | Uninfected Patients (n=71) | P-value |
|---------------|---------------------|-------------------------|---------------------------|---------|
| Demographics | 52.4 ± 21.8 years | 50.6 ± 13.4 years | 53.0 ± 23.6 years | 0.087 |
| Baseline malignancy, n (%) | 30 (20) | 10 (50) | 20 (29) | 0.034 |
| Non-Hodgkin Lymphoma (NHL) | 30 (20) | 10 (50) | 20 (29) | 0.034 |
| Acute lymphoblastic leukemia (ALL) | 7 (4) | 2 (10) | 5 (7) | 0.025 |
| Hematologic parameters prior to CTI | | | | |
| ANC median (Q1-Q3) | 0 (0-0.9) | 0.8 (0-2.5) | 0.6 (0-1.2) | 0.925 |
| Erythrocytes median (Q1-Q3) | 4.1 (3.6-4.6) | 4.2 (3.8-4.7) | 4.1 (3.6-4.6) | 0.830 |
| Antimicrobial prophylaxis prior to CTI, n (%) | 31 (34) | 12 (60) | 19 (27) | 0.004 |
| Antibacterial prophylaxis | 31 (34) | 12 (60) | 19 (27) | 0.004 |
| Antifungal prophylaxis | 29 (32) | 11 (55) | 18 (25) | 0.060 |
| Antimicrobial prophylaxis | 31 (34) | 12 (60) | 19 (27) | 0.004 |
| Anti-Pneumocystis prophylaxis | 6 (7) | 3 (15) | 3 (4) | 0.347 |
| Total length of stay, median (Q1-Q3) | 21 (20-22) | 24 (22-26) | 20 (22) | 0.238 |
| Length of stay from CTI, median (Q1-Q3) | 16 (15-16) | 16 (15-16) | 16 (15-16) | 0.316 |
| ICU admission, n (%) | 32 (35) | 13 (65) | 19 (27) | 0.003 |
| Length of ICU stay, median (Q1-Q3) | 4 (4-8) | 5 (4-8) | 4 (4-8) | 0.410 |
| Cytokine release syndrome (CRS), n (%) | 13 (15) | 5 (25) | 8 (11) | 0.231 |
| Grade 1-2 | 16 (18) | 7 (35) | 9 (13) | 0.010 |
| Grade 3-5 | 7 (8) | 4 (20) | 3 (4) | 0.015 |
| Toxicity of administration due to CTI, n (%) | 16 (18) | 6 (30) | 10 (14) | 0.050 |
| Toxicity of dose administration, median (Q1-Q3) | 0 (0-2) | 2 (1-4) | 0 (0-2) | 0.001 |
| Steroids administration due to CRS, n (%) | 13 (15) | 5 (25) | 8 (11) | 0.273 |
| Duration of care, median (Q1-Q3) | 10 (8-15) | 10 (8-15) | 10 (8-15) | 0.625 |

Table 3. Patients with Culture-positive Cholangitis after Kasai Portenterostomy (n=7).

Case No. | Antibiotic Prophylaxis | Time After Kasai (months) | Blood Culture | Resistance | Living or Decrease |
|---------|------------------------|---------------------------|---------------|------------|------------------|
| 1 | TMP-SMX | 4 | H. influenzae (non-Hib, no Beta-lactamase) | N/A | Living |
| 2 | TMP-SMX | 1.5 | E. coli | TMP-SMX | Living |
| 3 | TMP-SMX | 6 | K. pneumoniae | TMP-SMX | Living |
| 4 | TMP-SMX | 2 | E. coli | None | Living |
| 5 | TMP-SMX | 2.5 | E. coli | TMP-SMX | Ciprofloxacin | Living |
| 6 | TMP-SMX | 3.5 | E. coli | TMP-SMX | Ciprofloxacin | Living |
| 7 | TMP-SMX | 7 | E. coli | TMP-SMX | Ciprofloxacin | Living |
Conclusion: Antibiotic prophylaxis was frequently used after KP with TMP-SMX being the most common antibiotic used. Patients in the no-prophylaxis group had significantly lower Clostridioides difficile infections compared to those receiving antibiotic prophylaxis. Prophylactic antibiotics did not have an impact on time to recovery. Our findings suggest that prophylaxis is not helpful in decreasing the frequency of Clostridioides infections after KP and may increase the risk for infections with resistant bacteria. Larger prospective randomized control studies are recommended.

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580. Refractory and Resistant CMV Infections in Hematopoietic Cell Transplant Recipients in the Letermovir Primary Prophylaxis Era

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There was a trend towards lower all-cause mortality at day 100 in the letermovir group there was no resistant CMV and no CMV-related mortality in the letermovir group. This study aims at exploring the effect of letermovir primary prophylaxis on the occurrence of refractory or resistant CMV infections.

Methods: This is a single-center, retrospective cohort study of 537 consecutive allo-HCT CMV-seropositive recipients cared for between March 2016 and December 2018. Baseline demographics, transplant characteristics, CMV infections, treatment and mortality data were collected from the electronic medical record (Table 1). CMV outcomes were defined according to the standardized definitions for clinical trials. The primary emphasis was on outcomes defined according to the standardized definitions for clinical trials. Analysis, primary prophylaxis with letermovir was associated with a reduction in refractory or resistant CMV infection (OR 0.11, 95% CI 0.02–0.49) (Table 2). Notably, there was no resistant CMV and no CMV-related mortality in the letermovir group.

Results: Out of 537 patients identified, 123 received letermovir for primary prophylaxis during the first 100 days post-HCT and 414 did not. In a multivariate analysis, primary prophylaxis with letermovir was associated with a reduction in refractory or resistant CMV infections with resistant bacteria. Larger prospective randomized control studies are recommended.

Conclusion: Our study showed a strong association between primary prophylaxis with letermovir and reduction in refractory or resistant CMV infections and CMV disease in allo-HCT recipients.

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Table 2 - Multivariate Analysis of Clinical Outcomes.  

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Results: One hundred six patients met the inclusion criteria. The majority of patients received metronidazole (88 vs. 18). Less patients in the metronidazole arm developed aGVHD (51.1% vs 61.1%, p=0.44). In the subcategories of liver, skin, and gastrointestinal aGVHD, patients who received metronidazole developed less gastrointestinal aGVHD (26.1% vs 50.0%, p=0.045). Gastrointestinal ADEs were the most common metronidazole-related ADEs (19.3%, Table 1). There were no significant differences in the incidence of C. difficile infection, mortality, and overall survival between the two arms (Table 2).

Table 2. Additional Secondary Outcomes

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Conclusion: Despite a reduction in gastrointestinal aGVHD in the metronidazole arm, approximately one in four patients experienced an ADE to the medication, likely due to the prolonged use of the medication (33 days). The utilization of post-transplant cyclophosphamide for GVHD prophylaxis likely eliminates the need for metronidazole; however our findings suggest a benefit in preventing gastrointestinal aGVHD with metronidazole; albeit, caution is warranted given the high incidence of ADE associated with prolonged use.

Disclosures: All Authors: No reported disclosures

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Poster 400. Risks versus Benefits of Metronidazole Use for the Prevention of Acute Gvhd in Allogeneic Stem Cell Transplant Recipients

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Session: P-22. Care Strategies for Transplant Patients

Background: Currently, acute graft versus host disease (aGVHD) prophylaxis in hematopoietic stem cell transplants (HSCT) varies amongst different institutions. There is a lack of data supporting the use of metronidazole for aGVHD prophylaxis in HSCT. To further investigate if metronidazole has an effect on aGVHD, allogeneic HSCT recipients will be examined to determine if metronidazole post-transplantation decreases the incidence of aGVHD and the risks of adverse drug events (ADE) associated with this practice.

Methods: This retrospective study included 120 adult patients who received an allogeneic HSCT between January 1, 2010 to December 31, 2013. The primary endpoint is the incidence of aGVHD, defined as within 100 days post-transplant. Secondary endpoints include the rate of metronidazole discontinuation due to intolerance, frequency of metronidazole-related adverse effects, incidence of Clostridioides difficile infection, mortality, and overall survival.

Results: One hundred six patients met the inclusion criteria. The majority of patients received metronidazole (88 vs. 18). Less patients in the metronidazole arm developed aGVHD (51.1% vs 61.1%, p=0.44). In the subcategories of liver, skin, and gastrointestinal aGVHD, patients who received metronidazole developed less gastrointestinal aGVHD (26.1% vs 50.0%, p=0.045). Gastrointestinal ADEs were the most common metronidazole-related ADEs (19.3%, Table 1). There were no significant

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