7. Post-transplant infectious disease considerations

Table of Contents:

7.1 Viral
- 7.1.1 Cytomegalovirus
- 7.1.2 Epstein-Barr Virus and lymphoproliferative disorder
- 7.1.3 Herpes Simplex and Varicella-Zoster virus
- 7.1.4 Adenovirus infection
- 7.1.5 HBV prophylaxis and treatment
- 7.1.6 HCV prophylaxis and treatment
- 7.1.7 Arenavirus and West Nile Virus
- 7.1.8 BK Polyomavirus
- 7.1.9 Human Parvovirus
- 7.1.10 RNA Respiratory Viruses
- 7.2.11 Measles

7.2 Bacterial
- 7.2.1 Central venous catheter infections and treatment options
- 7.2.2 Mycobacterium tuberculosis
- 7.2.3 Non-tuberculosis mycobacterium
- 7.2.4 Nocardia

7.3 Fungal
- 7.3.1 PJP
- 7.3.2 Aspergillus
- 7.3.3 Cryptococcus
- 7.3.4 Invasive Candidiasis
- 7.3.5 Histoplasmosis

7.4 Other
- 7.4.1 Timing of post-transplant infections
- 7.4.2 Infectious exposure management
  - 7.4.2.1 Measles
  - 7.4.2.2 Varicella
  - 7.4.2.3 Influenza
  - 7.4.2.4 Tuberculosis
  - 7.4.2.5 Bacterial Meningitis
- 7.4.3 Immunizations
- 7.4.4 Toxoplasmosis prophylaxis and treatment

7.1 Viral

7.1.1 Cytomegalovirus
- Randomized, open label, multicenter study comparing everolimus to mycophenolic acid to determine whether treatment with everolimus could decrease incidence of CMV DNAemia and disease. At 6 months post transplant, 48% everolimus treated patients met the composite
endpoint (CMV DNAemia, CMV treatment, graft loss, death, discontinuation of study) versus 81% mycophenolate treated patients.

- Single center study comparing incidence of breakthrough CMV in transplant recipients while on letermovir prophylaxis vs valganciclovir prophylaxis. Also includes an evaluation of the drug interaction found with letermovir and tacrolimus.

- Review of 20 studies published on utilization of CMV-specific cell mediated immunity in solid organ transplant recipients.

- Multicenter retrospective review including CMV-seropositive kidney transplant recipients who did not receive T-cell depleting induction therapy that compared outcomes among those who received valganciclovir prophylaxis and those who did not. No difference in incidence of CMV disease, rejection, graft survival, or patient survival was found between groups.

- Case series of two kidney transplant recipients with emergence of letermovir resistance when used for secondary prophylaxis of ganciclovir-resistant CMV.

- Review of letermovir and Maribavir and their roles in the prevention of CMV in solid organ and stem cell transplant recipients.

- Retrospective review of pITR treated with valganciclovir evaluating the resolution of CMV viremia. 89% of patients had resolution of CMV viremia at an average dose of 14.3 mg/kg twice daily.

Retrospective analysis describing the incidence, risk factors, and clinical outcome of CMV, EBV, BKV, and JCV viremia in a cohort of pediatric allograft recipients treated with a corticosteroid-minimization regimen. Over the first 4 years post-transplant, the incidences of viremia were as follows: CMV, 25.5%; EBV, 52.0%; JCV, 16.3%; BKV, 26.5% with younger children at the time of transplant being more likely to develop EBV and BKV viremia.


Randomized clinical trial comparing the incidence of CMV disease in those high risk CMV liver transplant recipients who received preemptive therapy with valganciclovir 900mg twice daily to antiviral prophylaxis with valganciclovir 900mg daily.


Retrospective, single center study comparing early (< 72 hours post-transplant) versus delayed (> 72 hours post-transplant) initiation of CMV prophylaxis. Outcomes assessed included incidence of CMV infection, CMV disease, and cost analysis.


Most recent guidelines on the prevention and management of CMV in solid organ transplant recipients.


Single-center, retrospective study of five stem cell and organ transplant recipients who received letermovir for the treatment of refractory or resistant CMV infections.


Case series of four patients with ganciclovir-resistant CMV retinitis treated with letermovir.


Authors investigated utility of variable length valganciclovir prophylaxis as determined by the Quantiferon-CMV assay and found this method significantly reduced incidence of CMV infection.

- Phase II, open-label clinical trial comparing maribavir versus valganciclovir in recipients of hematopoietic-cell or solid organ transplants with CMV reactivation


- A report summarizes the recommendations of an international panel of experts who convened in March 2017 to revise and expand evidence and expert opinion-based consensus guidelines on CMV management


- Phase II clinical trial comparing the efficacy, safety, and immunogenicity of ASP0113 (n=75) versus placebo (n=74); did not demonstrate efficacy in prevention of CMV viremia


- Long-term follow-up (up to 84 months) of above study comparing valganciclovir as primary prophylaxis to preemptive therapy in kidney transplant recipients who were of intermediate risk


- This study reviews the impact of pharmacist intervention adjusting valganciclovir dosing for CMV prophylaxis. The primary endpoint was CMV infection and ganciclovir resistance in a pre-intervention vs post-intervention group.


- Retrospective cohort of patients with CMV with U97 gene conferring ganciclovir resistance reviewing the treatment and clinical course patients experienced.


- Phase III, double-blind trial of CMV seropositive allogeneic hematopoietic-cell transplant recipients comparing letermovir to placebo for CMV prophylaxis

Fleming J, et al. (2017). Valganciclovir (VGCV) followed by cytomegalovirus (CMV) hyperimmune globulin compared to VGCV for 200 days in abdominal organ transplant recipients at high risk for CMV infection: A...

- Prospective, randomized, open-label pilot study comparing valganciclovir prophylaxis for 200 days vs VGCV for 100 days followed by CMV hyperimmune globulin in abdominal transplant recipients at high risk for CMV


- A review article that discusses the management and prevention of CMV with elaborations on the new advances in the development of new antivirals, adoptive immunotherapy and DNA-CMV vaccines that might transform the management of CMV in the near future.


- A study that test the role of IL-10 being an indicator for the risk of development of CMV infection after prophylaxis, and hence guiding the needed length of prophylaxis in kidney and liver transplant recipients


- The pediatric dosing algorithm for VGCV (utilizing individuals' body surface area and renal function) provides systemic GCV exposures in patients younger than 4 months that are similar to those observed in older pediatric populations. The data indicate that this dosing algorithm is appropriate across the entire pediatric age range, including this youngest age group.


- Use of everolimus was associated with a significantly lower rate of CMV infection compared to azathioprine or mycophenolate (OR 0.19, 95% C.I. 0.09-0.39; p<0.0001)


- British guidelines on the recommendations on the prophylaxis and treatment options of CMV in solid organ transplant.

Systematic review of the literature included randomized clinical trials investigating clinical outcomes of prophylactic polyvalent immunoglobulin or cytomegalovirus (CMV)-specific immunoglobulin or plasma in patients undergoing HSCT. Clinical outcomes included overall survival, transplant-related mortality, CMV infection, CMV disease, graft-versus-host disease, interstitial pneumonitis/fibrosis and hepatic veno-occlusive disease.


Critical review based on relevant articles published about CMV infection in renal transplant elaborating on different clinical aspects, including resistance to ganciclovir.


A multicenter, retrospective study found that low-dose and high-dose valganciclovir regimens provide similar efficacy in preventing CMV disease in high-risk renal transplant recipients. Low-dose valganciclovir group had reduced incidence of leukopenia associated and may provide a significant cost avoidance benefit.


An overview of the contemporary epidemiology, clinical presentation, diagnosis, prevention and treatment of CMV infection in solid organ transplant recipients.


Summary of CMV risk factors, CMV prophylaxis and CMV treatment options from the AST Infectious Disease Community of Practice.


Phase II clinical trial comparing CMV treatment with standard of care vs letermovir in kidney alone or kidney-pancreas transplant recipients with active CMV viral replication.


The impact of valganciclovir as primary prophylaxis compared to preemptive therapy on rates of cytomegalovirus (CMV) infection and disease occurrence was evaluated in kidney transplant recipients who were of intermediate CMV risk.

- A meta-analysis that included all studies evaluating valganciclovir 900 mg and 450 mg daily against controls as CMV prophylaxis in a direct comparison. Valganciclovir 900 mg showed no superiority efficacy compared to controls (ganciclovir or preemptive) and equivalent efficacy to VGC 450 mg for CMV universal prophylaxis. VGC 900 mg was significantly associated with 3 times increase in the risk of leukopenia and 2 times increase in the risk of rejection compared with VGC 450 mL


- A single-center study on subset of patients whom were initially enrolled in a prospective, randomized, placebo-controlled study of CMV prevention in lung transplantation. The study aimed to determine if extended prophylaxis conferred a sustained long-term benefit and to assess its hematologic safety. It showed that extending valganciclovir prophylaxis to 12 months provides a durable long-term CMV protective benefit compared with short-course therapy, without increasing adverse hematologic effects


- Multicenter Randomized, clinical trial involving 11 U.S. lung transplant centers, to determine whether extending prophylaxis with oral valganciclovir from the standard 3 months to 12 months after lung transplantation is efficacious. A beneficial effect with regard to prevention of CMV disease seems to extend at least through 18 months after transplantation


- CMV disease at 1 year was evaluated in high-risk kidney transplant recipients on valganciclovir prophylaxis for 100 days compared to 200 days.


- International, randomized, prospective, double-blind study, compared 318 CMV D+/R- kidney transplant recipients receiving valganciclovir (900 mg) once daily for up to 200 days vs. 100 days. Long-term outcomes including CMV disease, acute rejection, graft loss, patient survival, and seroconversion were assessed

• Single-center, retrospective study that reports on its use in 17 transplant recipients with complex CMV syndromes who had failed or were intolerant to other therapies


• 1-year follow-up of VICTOR study, 321 SOT recipients with CMV disease were followed 1 year after treatment with either twice daily intravenous ganciclovir or oral valganciclovir (for 21 days) followed by once daily valganciclovir until day 49 in all patients


• Meta-analysis included 11 articles which evaluated the impact of cytomegalovirus (CMV) immune globulin on CMV disease prevention and rejection.


• Preemptive valganciclovir therapy was compared to valacyclovir prophylaxis for their impact on cytomegalovirus disease and acute rejection at 12 months following kidney transplantation.


• A randomized, international trial (VICTOR study), recipients with cytomegalovirus disease were treated with either 900 mg oral valganciclovir or 5 mg/kg i.v. ganciclovir twice daily for 21 days, followed by 900 mg daily valganciclovir for 28 days. A total of 321 patients were evaluated. Oral valganciclovir shows comparable safety and is not inferior to i.v. ganciclovir for treatment of cytomegalovirus disease in organ transplant recipients and provides a simpler treatment strategy.


• A Meta-analysis that included 17 trials and 9 trials on universal prophylaxis and preemptive therapy, respectively, and evaluated the effectiveness of the various approaches in reducing the incidence of CMV disease.


• Oral valganciclovir prophylaxis was compared to preemptive valganciclovir therapy for its pharmacoeconomic impact and occurrence of cytomegalovirus infection.

- A case report on a 1S-year-old boy with juvenile myelo-monocytic leukemia (JMML) received an allogeneic HSCT with bone marrow stem cells from a mismatched, unrelated donor. He who had refractory CMV infection despite the treatment with cidofovir. A rapid decline of his CMV-copy number and successful treatment was achieved with the combination foscarnet/leflunomide.


- In this randomized, prospective, double-blind, double-dummy study, 364 CMV D+/R- patient received valganciclovir 900 mg once daily or oral ganciclovir 1000 mg three times a day (TID) within 10 days of transplant and continued through 100 days. It looked at development of CMV disease and CMV viremia during 6 & 12 months. Also, Time- on of CMV disease and to viremia was compared.


- A prospective study that determined the safety and efficacy of valganciclovir or prevention of cytomegalovirus (CMV) in at-risk (donor positive/recipient negative [D+/R-] or R+) lung transplant recipients, and determined the length of prophylaxis required to significantly decrease both CMV infection and disease all in consecutive lung transplant recipients surviving >30 days. It showed that valganciclovir is safe and effective for prevention of CMV infection and disease in at-risk lung transplant recipients. The required length of prophylaxis was at least 180 days.


- Placebo-controlled trial evaluating valacyclovir prophylaxis for prevention of cytomegalovirus disease in kidney transplant recipients.

7.1.2 Epstein-Barr Virus and Lymphoproliferative disorder


- Retrospective analysis evaluating incidence of PTLD in heart transplant patients receiving sirolimus based immunosuppression. Conversion to sirolimus was found to be protective against development of PTLD in this population.

- Review of 11 studies including a total of 76 solid organ transplant recipients who received treatment for PTLD with EBV-specific cytotoxic T lymphocytes. The review concluded that therapy with EBV-specific cytotoxic T lymphocytes is safe and effective in PTLD.


- The American Journal of transplantation guidelines for management of Epstein-Barr Virus and Posttransplant Lymphoproliferative Disorder in Solid Organ Transplantation


- Review article of epidemiology, presentation, diagnosis, and treatment of PTLD.


- Review article describing antiviral drugs used to inhibit EBV replication


- Systematic review and meta-analysis of antiviral prophylaxis for the prevention of PTLD in EBV seronegative patients receiving organs from EBV seropositive donors.


- Small randomized, double-blind, placebo-controlled study evaluating the effects of valganciclovir on oral EBV shedding


- Evidence-based recommendations for diagnosis, prevention, prophylaxis and therapy of post-transplant lymphoproliferative disorders exclusively in the stem cell transplant setting


- A single, large-volume center assessed the incidence, predictors and outcomes of PTLD after liver transplantation. Suggested switching immunosuppression from calcineurin inhibitor to sirolimus may improve survival.
- A multicenter retrospective study assessed the impact of rituximab on the outcome of PTLD. They examined the clinical features and outcomes among a large cohort of solid organ transplantation (SOT) patients with PTLD.

- A multicenter retrospective study analyzed the incidence of post-transplant non-Hodgkin lymphoma in 44,828 recipients of deceased-donor kidney transplants who were reported to the scientific registry of the Collaborative Transplant Study. Patients had received antiviral drugs (aciclovir or ganciclovir) or anti-CMV immunoglobulin to prevent CMV infection according to the transplant centres' protocols, or no CMV prophylaxis.

- A multi-center trial assessing two different regimens and their effect on EBV replication. EBV D+/R- solid organ transplant recipients were randomized to receive either ganciclovir and placebo or ganciclovir and immunoglobulin (IG) for 3 months. No significant difference in EBV viral load suppression was observed when ganciclovir was compared with ganciclovir and IG in high-risk EBV D+/R- patients.

- A randomized controlled trial assessing CMV-IVIG (cytomegalovirus-intravenous immunoglobulin) for prevention of Epstein Barr virus (EBV) posttransplant lymphoproliferative disease (PTLD) in pediatric liver transplantation (PLTx) recipients was begun in Pittsburgh and subsequently expanded to four additional sites. Patients were followed for 2 years post-LTx. No significant differences were seen in the adjusted 2-year EBV disease-free rate and PTLD-free rate between treatment and placebo groups at 2 years.

7.1.3 Herpes Simplex and Varicella-Zoster virus
- Retrospective, single center study of pediatric liver transplant recipients describing long term immunity over 10 years, including the influence of booster vaccinations.

- Case study of donor-derived herpes simplex virus hepatitis in a kidney transplant recipient and a review of eight previously published case studies.

- Review of 12 observational studies including 6560 solid organ transplant recipients that assessed the incidence of post-transplant herpes zoster infections across various organs.


- Randomized, observer-blind, multicenter trial of 234 renal transplant recipients comparing the immunogenicity and safety of recombinant zoster vaccine (RZV) to placebo.


- The American Journal of Transplantation guidelines on the management of herpes simplex virus in solid organ transplantation


- The American Journal of Transplantation guidelines on the management of varicella zoster virus in solid organ transplantation


- Retrospective study of 85 children undergoing renal transplant assessing clinical outcomes in patients who had the VZV infection pre-transplant compared to those who received vaccination pre-transplant


- Report detailing 5 clusters of donor-derived HSV-2 infection in donor positive, recipient negative solid organ transplant, the treatment of HSV and clinical outcomes of infection.


- Evidence-based guidelines of the European Conference on Infections in Leukemia recommendations for managing of HSV, VZV and EBV infections in leukemia patients and in stem cell transplant recipients

Arora A et al. (2008). Double-blind study comparing 2 dosages of valacyclovir hydrochloride for the treatment of uncomplicated herpes zoster in immunocompromised patients 18 years of age and older.
● No differences in median time to full healing of HSV rash were detected among patients receiving valacyclovir 1 gram TID versus 2 grams TID


● A double-blind controlled trial, 77 hematopoietic cell transplant recipients at risk for VZV reactivation were randomized to acyclovir 800 mg twice daily or placebo given from 1 to 2 months until 1 year after transplantation. VZV disease at 1 year was the primary end point


● A meta-analysis of 12 randomized trials (1574 patients) examined herpesvirus (CMV, VZV, HSV) and related outcomes following organ transplantation over a range of acyclovir exposures (including valacyclovir)


● Famciclovir 500 mg three times a day was compared to acyclovir 800 mg five times a day showed no significant difference in new lesion formation, time to healing or duration of pain were observed


● Acyclovir limited cutaneous dissemination as well as abbreviated duration of positive cultures, pain associated with lesions, postulation of lesions, crusting of lesions and complete healing of lesions.

7.1.4 Adenovirus infection


● The American Journal of Transplantation guidelines for the diagnosis and management of Adenovirus in solid organ transplantation

Physician surveys conducted to determine current adenovirus screening and treatment practices at their center


Randomized, placebo-controlled phase II trial evaluating preemptive treatment with brincidofovir for the prevention of adenovirus disease in pediatric and adult allogeneic HCT recipients with asymptomatic adenovirus viremia


A review on the management of pediatric patients with adenovirus infection post-transplant pediatric patients.

7.1.5 HBV prophylaxis and treatment

Multicenter, retrospective study evaluating prevalence of HBV reactivation in HBsAg negative, anti-HBc-positive kidney transplants who did or did not receive HBV prophylaxis. Study suggests that prevalence HBV reactivation in this cohort is low regardless of prophylaxis.


Prospective trial evaluating a perioperative Hepatitis B virus (HBV) prophylaxis regimen in pediatric liver transplant patients receiving a HBV core antibody positive (HBcAb) graft. Patients needed a HbsAb serum titer of 1000 IU/L or more pre-transplant (were vaccinated if not) and needed to maintain a HbsAb titer of 200 IU/L post-transplant (would receive Hepatitis B immunoglobulin if not). Graft and survival rates were not significantly different between patients who received an HbcAb+ versus a HbcAb- graft. Patients who met pre- and/or post-operative HBsAb criteria had a lesser incidence of de novo Hepatitis B infection post-transplant. Infection rate in those meeting both criteria was 1.3%, those with only pre-operative criteria was 4.2%, those with only post-operative criteria was 1.9%, and those meeting neither criteria was 43.8%. Authors concluded that their prophylactic strategy was effective at preventing de novo Hepatitis B infection in HbcAb+ liver graft recipients.


A review of current practices for kidney transplants using hepatitis B positive donors including a summary of long-term outcomes.

The American Society of Transplantation's practice guidelines for preventing and treating viral hepatitis in solid organ transplant recipients.


Retrospective study describing impact of hepatitis B core antibody positive liver grafts on survival and risk of de novo HBV infection


The European Association for the Study of Liver practice guidelines for treating individuals chronically infected with the hepatitis B virus.


Phase III, open-label, single arm study evaluating Hepabulin HBIG and its effect on preventing Hepatitis B seroconversion in naïve liver transplant recipients.


Retrospective review of hepatitis B core antibody positive liver transplant recipients comparing use of hepatitis B immunoglobulin, antivirals, or combination


Described long-term outcomes of 265 consecutive chronic hepatitis B liver transplant recipients treated with entecavir monotherapy.


The American Association for the Study of Liver Diseases (AASLD) recommendations on the treatment of chronic hepatitis B virus infection in adults and children in compliance with the Institute of Medicine standards for trustworthy practice guidelines


Updated recommendations on when to treat, when to monitor, what patients should receive HBV therapy, and what drugs should be selected for each scenario


A recent review article discussing Strategies for prevention of HBV after LT

- A review article that discusses the management of Chronic hepatitis B virus (HBV) infection post liver transplantation in the presence of newer more potent oral antiviral agents associated with less resistance (e.g., entecavir and tenofovir) for the treatment of CHB either in combination with HBIG or alone as a monotherapy.


- Another review article that discusses the management of chronic hepatitis B before and after liver transplantation


- The impact of entecavir, adefovir, and lamivudine therapy on virologic and biologic responses in hepatitis B surface antigen positive kidney transplant recipients is evaluated.


- Case series evaluating the use of entecavir or adefovir in kidney transplant recipients with hepatitis B virus infection resistant to lamivudine.


- The European Association for the Study of Liver discuss preventing and treating viral hepatitis (HBV, HCV and HEV) in solid organ transplantation other than liver transplantation


- A review article that describe the diagnosis, prevention and management of HBV infection in allogeneic hematopoietic stem cell transplant candidates, from the pre- to post-transplant period.


- The impact of long term antiviral therapies (lamivudine, tenofovir, adefovir) on hepatitis B virologic response and liver disease was evaluated in heart transplant recipients.

The prospective trial evaluates the use of adefovir dipivoxil in addition to lamivudine therapy for treating patients with chronic hepatitis B who developed a resistant strain of the hepatitis B virus. Hepatitis B viral load response to combination treatment was evaluated in patients with compensated as well as decompensated disease.


The prospective, open-label trial evaluates the strategies for preventing hepatitis B virus recurrence following liver transplantation. Patients received lamivudine in addition to hepatitis B immune globulin as combination therapy for the first month following transplant and were then randomized to receive either combination therapy for 17 months or lamivudine monotherapy for 17 months.


An open-label, multicenter, international study that evaluated the impact of adefovir in pre- and post-liver transplant recipients on hepatitis B viral load was evaluated in patients with lamivudine-resistant hepatitis B.

7.1.6 HCV prophylaxis and treatment


Systematic review with meta analysis of nonviremic recipients of heart transplants that had HCV viremic donors. Authors concluded that excellent clinical outcomes have been achieved in this population.


Review of HCV epidemiology, clinical outcomes, HCV treatment, studies on transplantation from positive donors to negative recipients, and evolving clinical management.


Review of 11 studies including 201 patients on the safety and efficacy of kidney transplant from HCV-viremic donors into HCV naïve recipients and the use of direct-acting antiviral agents in these patients.

- Review on the practice of transplanting HCV-viremic organs into HCV naïve recipients, including a discussion of the barriers to implementation.


- Review of published literature on safety and feasibility of transplanting HCV-viremic organs into HCV naïve recipients.


- Multicenter, randomized, double-blind, placebo-controlled trial of emricasan in HCV liver transplant recipients with residual fibrosis or cirrhosis after achieving sustained virologic response to HCV therapy.


- Review of studies and registry data for the use of HCV-positive donors in heart transplantation.


- Single-center trial to determine safety and efficacy of ultra-short-term perioperative pangenotypic DDA prophylaxis for decease HCV NAT positive donors to HCV negative kidney transplant recipients.


- Case series of 44 HCV-uninfected heart and lung transplant recipients who received HCV-viremic organ transplants and preemptive treatment with sofosbuvir-velpatasvir


- Open-label nonrandomized trial of 10 HCV-uninfected kidney transplant recipients receiving kidneys from HCV-infected donors and receiving DAAs as prophylaxis before and after kidney transplantation


- World health organization guidelines for screening and treatment of chronic hepatitis C infection

- The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America practice guidelines for testing and treating hepatitis C virus infection


- Cohort study based on data from the European Liver Transplant Registry (ELTR) analyzing evolution of indications and results of liver transplantation over 10 years in Europe, focusing on the changes induced by the advent of DAAs


- The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America practice guidelines for testing and treating hepatitis C virus infection.


- Prospective cohort study of HCV antibody-negative or NAT negative liver transplant recipients who received a liver graft from donors who were HCV antibody positive but NAT negative


- Case series of thirteen patients undergoing heart transplant using hepatitis C-positive donors


- Describes 12-month HCV treatment outcomes in an open-label, nonrandomized single center study of 20 HCV-negative transplant candidates (including the ten recipients of the THINKER-1 study)


- Correspondence to the editor describing results of the THINKER study, an open-label, single-group, pilot trial at University of Pennsylvania


- Consensus document regarding availability and use of Hepatitis C positive donor organs as well as transmission and payor concerns.

• Short communication reporting the use of increased risk donor organs. Describes a higher rate of use of increased risk donor organs compared to national rate of use.


• SRTR registry study analyzing the impact of DAAs on utilization and outcomes associated with HCV-positive deceased donor kidney transplant


• Phase II, open label study investigating combination of simeprevir (SMV), daclatasvir (DCV), and ribavirin (RBV) administered for 24 weeks in 35 patients with recurrent HCV genotype 1b infection after orthotopic liver transplantation.


• Retrospective, single-center study of liver transplant recipients who received ledipasvir/sofosbuvir without ribavirin for treatment of recurrent hepatitis C.


• Chronic hepatitis C infection is associated with a significantly increased post-transplant mortality in heart transplant recipients. The introduction of new direct-acting antiviral agents may provide a treatment option for HCV pre- or post-heart transplantation which could have a positive impact on patients’ survival.


• Retrospective, single-center, cohort analysis of kidney transplant recipients who received direct-acting antivirals for treatment of Hepatitis C. Endpoints included SVR at 12 weeks post completion of therapy and allograft function.


• Correspondence to the editor describing an open-label, multicenter, phase 2 study involving wait-listed patients with chronic HCV genotype 1 infection who were undergoing a first liver transplantation from an HCV-negative donor

● Review article of the data on direct acting antivirals combination therapies in transplantation, discuss the advantages and disadvantages of pre vs. post-transplant HCV therapy and future directions


● A review article on the management of post liver transplant hepatitis C infection


● A review article that discuss the recent studies that have emerged on the use of NS5b polymerase inhibitor, sofosbuvir in combination with second generation protease inhibitor, simeprevir, fixed dose ledipasvir or daclatasvir with or without ribavirin in the treatment of post-transplant rHCV infection


● A retrospective study examining the "real world" treatment of 170 patients with chronic HCV genotype 1 using the combination of SMV and SOF with or without ribavirin (RBV) for a fixed 12-week duration irrespective of prior interferon therapy, transplant status or fibrosis stage. The data confirm excellent SVR outcomes with favorable safety and tolerability profiles in patients who carry many traditional high-risk features for non-response, including post-LT recipients and patients with advanced liver disease


● The open-label ALLY-1 study assessed the safety and efficacy of a 60-mg once-daily dosage of daclatasvir (pan-genotypic NS5A inhibitor) in combination with sofosbuvir at 400 mg once daily (NS5B inhibitor) and ribavirin at 600 mg/day for 12 weeks with a 24-week follow-up in two cohorts of patients with chronic HCV infection of any genotype and either compensated/decompensated cirrhosis or post transplantation recurrence


● A report of efficacy and safety data for DCV-based all-oral antiviral therapy in liver transplantation (LT) recipients with severe recurrent HCV. DCV at 60 mg/day was administered for up to 24 weeks as part of a compassionate use protocol for 97 infected patients.

This article describes the experience with DAAs in the treatment of posttransplant genotype (GT) 1 HCV from a consortium of community and academic centers (Hepatitis C Therapeutic Registry and Research Network [HCV-TARGET]). Twenty-one of the 54 centers contributing to the HCV-TARGET consortium participated in this study. Enrollment criteria included positive posttransplant HCV RNA before treatment, HCV GT 1, and documentation of use of a simeprevir (SMV)/sofosbuvir (SOF) containing DAA regimen. Safety and efficacy were assessed. A total of 162 patients enrolled in HCV-TARGET started treatment with SMV+SOF with or without ribavirin (RBV) following LT.


An ongoing, prospective, partially-randomised, phase 2, open-label study of once-daily SMV 150 mg + sofosbuvir 400 mg with and without ribavirin (RBV) 1000 mg (1200 mg for subjects ≥75 kg) in subjects with recurrent genotype 1 HCV post-orthotopic liver transplant


The first multicenter included 123 patients that reported the efficacy, safety, and tolerability of this regimen in LT recipients


A prospective, observational study that evaluated the efficacy of sofosbuvir and simeprevir in patients with genotype 1 HCV post-liver transplant. Patients received sofosbuvir 400 mg plus simeprevir 150 mg daily for 12 wk without ribavirin. The primary end point was a sustained virologic response 12 wk after the end of therapy.


A study that evaluated the efficacy and safety of sofosbuvir- and daclatasvir-based regimens. It analyzed data from 23 patients with Fibrosing cholestatic hepatitis who participated in a prospective cohort study in France and Belgium and the effects of antiviral agents in patients with recurrence of HCV infection after liver transplantation


A prospective, multicenter, open-label pilot study that evaluated the efficacy and safety of an interferon-free regimen of the nucleotide polymerase inhibitor sofosbuvir combined with ribavirin for 24 weeks in treating post-transplantation HCV infection

- The American society for blood and marrow transplantation task force recommendations in the management of HCV in HSCT donors and recipients


- An article that explores arguments for and against treating HCV in patients on the transplant list


- A phase 2, open-label study of 61 patients with HCV of any genotype and cirrhosis to determine whether sofosbuvir and ribavirin treatment before liver transplantation could prevent HCV recurrence post-transplant


- A phase 2, open-label study included enrolled 337 patients and assessed treatment with the NS5A inhibitor ledipasvir, the nucleotide polymerase inhibitor sofosbuvir, and ribavirin in patients infected with HCV genotypes 1 or 4


- A result of a study done with sofosbuvir (SOF) and ribavirin (RBV) on a compassionate-use basis to patients with severe recurrent hepatitis C, including those with fibrosing cholestatic hepatitis (FCH) and decompensated cirrhosis who had a life expectancy of 1 year or less. All patients received 24-48 weeks of SOF plus RBV. SOF and RBV provided high rates of SVR in patients with severe recurrent HCV, including patients with early severe recurrence, FCH, and cirrhosis.


- A phase 3, double-blind, placebo-controlled study involving untreated and previously treated patients with chronic HCV genotype 1, 2, 4, 5, or 6 infection, including those with compensated cirrhosis. Patients randomized to receive the nucleotide polymerase inhibitor sofosbuvir and the NS5A inhibitor velpatasvir in a once-daily, fixed-dose combination tablet or matching placebo for 12 weeks

A phase 3, open-label study involving both previously treated and previously untreated patients infected with HCV genotypes 1 through 6 who had decompensated cirrhosis. Patients were randomly assigned to receive velpatasvir once daily for 12 weeks, sofosbuvir-velpatasvir plus ribavirin for 12 weeks, or sofosbuvir-velpatasvir for 24 weeks. The primary end point was a sustained virologic response at 12 weeks after the end of therapy.


- Prospective, randomized trial evaluating ledipasvir and sofosbuvir therapy with or without ribavirin therapy for 12 or 24 weeks in 440 previously treated patients with hepatitis C virus genotype 1. Sustained virologic response at 12 following treatment was high among all treatment groups with no significant differences seen between groups.


- Prospective, randomized trial evaluating ledipasvir and sofosbuvir with or without ribavirin for 8 weeks or ledipasvir and sofosbuvir therapy for 12 weeks in 647 treatment-naïve patients with hepatitis C virus genotype 1. Sustained virologic response 12 weeks following treatment was high among all treatment groups with no significant differences seen between groups.


- Prospective, phase II trial evaluating simeprevir, ribavirin, and peginterferon combination therapy compared to ribavirin and peginterferon therapy in treatment-experienced patients with hepatitis C virus genotype 1. Simeprevir dosing (100mg vs. 150mg) and duration (12, 24, or 48 weeks) are evaluated with 48 weeks of peg-interferon and ribavirin therapy. Sustained virologic response 24 weeks following treatment was significantly higher in the simeprevir groups compared to the ribavirin and peginterferon group.


- The SOLAR-1 study was a large, multicenter, randomized controlled trial that included liver-transplant recipients (n=223) across a broad spectrum of histologic and clinical severity of recurrence. Study participants were randomly assigned to receive fixed-dose combination ledipasvir (90 mg) and sofosbuvir (400 mg) (hereafter ledipasvir/sofosbuvir) and weight-based ribavirin (1000 mg [<75 kg] to 1200 mg [≥ 75 kg]) for either 12 weeks or 24 weeks.


- The FISSION (N=499) and NEUTRINO (N=327) trials evaluate the use of sofosbuvir and ribavirin with (NEUTRINO) or without (FISSION) peginterferon for 12 weeks in hepatitis C virus infected patients who did not previously receive treatment. In the NEUTRINO trial, sustained virologic
response at 12 weeks following treatment (SVR 12) was 90% in patients with HCV genotype 1, 4, 5, or 6. In the FISSION trial, SVR 12 was 67% in patients with genotype 2 or 3.


- The POSITRON (N=278) and FUSION (N=201) trials evaluate the use of sofosbuvir and ribavirin for 12 weeks in hepatitis C virus infected patients with genotypes 2 or 3 who are either intolerant/had contraindication to peginterferon treatment (POSITRON) or failed peginterferon treatment (FUSION). Sustained virologic response 12 weeks following treatment was 78% and 50% in the POSITRON and FUSION trials, respectively.

7.1.7 Arenavirus and West Nile virus (WNV)


- American Society of Transplantation’s guidelines on Arenaviruses and West Nile viruses in the pre- and post-transplant period


- Case series of WNV infection in kidney and pancreas transplant recipients that compared their outcomes with the general population and discussed the utility of U.S. plasma-derived IVIG as an adjuvant therapy for immunocompromised patients with complicated WNV infection. Arenavirus is mainly managed with supportive care with meticulous fluid balance and electrolyte infection. Intravenous ribavirin is the drug of choice for Lassa fever and should be considered for the treatment of Argentine and Bolivian hemorrhagic fever.


- Therapeutic strategies of donor-derived WNV infection based on these 4 cases included supportive care, reduction of immunosuppression, and frequent intravenous immunoglobulin and interferon


- A review of 3 cases of kidney or pancreas transplants recipients who developed West Nile fever and had meningoencephalitis and review the literature on West Nile fever in organ transplant recipients

Report two recipients of cadaveric kidneys from a single donor showed that organ recipients receiving immunosuppressive drugs may be at high risk for severe disease after WNV infection and blood transfusion was the probable source of the West Nile virus viremia in the organ donor.

### 7.1.8 BK Polyomavirus


- Review of epidemiology of BKPyV infections in kidney transplant recipients and current evidence that supports screening and management strategies


- Review of the diagnosis and treatment of BK virus associated nephropathy. Includes summary of differences seen in pediatric patients as well as a treatment algorithm.


- Review of BK polyomavirus nephropathy after kidney transplant and the optimization of immunosuppression in this patient population.


- The American Society of Transplantation’s practice guidelines for preventing and treating BKV in solid organ transplant recipients.


- A 3-month course of ciprofloxacin early following transplantation did not prevent BK viremia but was associated with increased rate of fluoroquinolone-resistant infections


- Retrospective single-center study assessing long-term outcomes using standard operating procedure of treating BK polyomavirus based on first reducing calcineurin inhibitor

• Analysis of Cooperative European Pediatric Renal Transplant Initiative Registry describing the epidemiology and risk factors for BK polyomavirus in pediatric renal transplant recipients


• Observational retrospective study evaluating the impact of leflunomide treatment for BK polyomavirus associated nephropathy


• Single-center study assessing cut-off value of viremia that best discriminates the risk of progression to nephropathy


• A morphologic classification scheme for definitive PVN is described by the Banff Working Group on Polyomavirus Nephropathy


• This prospective study found that recipient BKV viruria prior to transplant predicts post-transplant viruria but not viremia or BKV nephropathy


• Retrospective analysis of BK polyomavirus screening and immunosuppression reduction demonstrating short-term decline in renal function but long-term benefits for graft function with early detection, prompt diagnosis, and reduction in immunosuppression


• Meta-analysis comparing incidences of cytomegalovirus and BK polyoma virus infections in renal transplant recipients receiving a mTOR inhibitor based regimen compared with a calcineurin inhibitor-based regimen


• A retrospective evaluation of kidney transplant recipients diagnosed with BK viruria treated with ciprofloxacin course following the initial reduction in immunosuppression showed that ciprofloxacin may be a useful therapeutic tool for BKV infection refractory to conventional treatment.
- A 3-month course of levofloxacin early following transplantation did not prevent BK viruria, but was associated with an increased risk of adverse events such as bacterial resistance

- Leflunomide therapy in addition to a reduction of the immunosuppressive therapies resulted in a significant decline in the BK viral load without further deterioration of renal function

- The use of everolimus to minimize calcineurin inhibitors was investigated in kidney transplant recipients. Over two years, a higher rate of CMV (infection, disease, and syndrome) and BKV was found in groups not receiving everolimus.

- From June 2004 – December 2008, 823 patients were retransplanted following BK nephropathy in prior kidney. Of these patients, 17.5% required treatment for BKV after retransplant.
- The 1 and 3 year Kaplan–Meier graft survival rates and median GFR were 98.5%, 93.6%, 65.5 and 68.4mL/min, respectively.

- Patients taking fluoroquinolones for one month after kidney transplant to prevent UTIs was associated with lower rates of BK viremia within 1-year post-transplant.

- A systemic review evaluated 40 studies looking at immunosuppression reduction and antivirals for the management of BKV. There is no graft survival benefit to adding leflunomide or cidofovir to immunosuppression reduction for the management of BKV.

- Kidney transplant patients with BKV were managed with immunosuppression reduction with or without cidofovir 1.0 mg/kg weekly for up to 10 weeks without probenecid. The Kaplan-Meier graft survival at 6 years was significantly improved in patients who received cidofovir.

From 2004 - 2006, 34,937 kidney transplant patients were reviewed for the diagnosis of treated BK virus (TBKV) and risk factors. TBKV was found in 1.6% and 2.6% of patients at 6 months 1 year after transplant respectively.

Risk factors for TBKV included advanced donor age, pediatric, African American and male recipients, HLA-mismatching, tacrolimus maintenance and Thymoglobulin induction as baseline immunosuppression.


- Treating BKV in kidney transplant recipients with leflunomide alone or leflunomide plus cidofovir resulted in graft loss of 15% with a follow-up time of 6-40 months.
- The target leflunomide metabolite (A77 1726) trough was 50 – 100 mcg/mL; leflunomide trough values of < 40 mcg/mL did not clear the virus until cidofovir was added or adequate leflunomide drug levels were attained.


- Kidney transplant patients received immunosuppression reduction and 2 g/kg of IVIG. After a mean follow-up of 15 months, 88% of patients still had functioning grafts.


- The use of BK viral monitoring and immunosuppression reduction kidney transplant recipients following the identification of viremia was associated with resolution of viremia and absence of BK nephropathy.
- BKV plasma PCR was collected pre-transplant, weekly for 16 weeks, and then at months 5, 6, 9, and 12.
- At the time of BKV identification, the antiproliferative was discontinued. If viremia did not clear within 4 weeks, the calcineurin inhibitor dose was decreased by 20-25%.


- Treating BKV in kidney transplant recipients with cidofovir 0.5–1.0 mg/kg weekly for 4-10 weeks with probenecid in addition to immunosuppression reduction resulted in renal function stabilization and no graft loss with a follow-up time of 8–41 months (median 24.8).


- Checking BKV DNA PCR in plasma from kidney transplant recipients is a sensitive (100%) and specific (88%) method for identifying viral nephropathy.

7.1.9 Human Parvovirus
Zhong Q, Zeng J, Lin T, Song T. (2022). The detection, treatment of parvovirus B19 infection induced anemia in solid organ transplants: A case series and literature review of 194 patients [published online

- Retrospective analysis of solid organ transplant recipients with parvovirus B19 infection to determine association with anemia and treatment modalities and literature review


- The American society of transplantation guidelines for management of Parvovirus in solid organ transplantation


- Multivariate analyses to identify risk factors of positive parvovirus B19 PCR results


- A review article that discusses the epidemiology, clinical manifestations, diagnosis and treatment of less common viruses (e.g.: West Nile virus, Parvovirus and human T-cell lymphotrophic virus) in the setting of kidney transplantation


- A review of 91 cases describing the epidemiology and clinical spectrum of posttransplant PVB19 infection over 16 years period, with literature review

7.1.10 RNA Respiratory Viruses


- Review of the epidemiology, clinical manifestations, prevention, and treatment of RNA and DNA respiratory viruses, excluding SARS-CoV-2.


- Review of the impact of COVID-19 on solid organ transplantation, including epidemiology, outcomes, diagnosis, and treatment of COVID-19 in this population.


- Review of the immune response to SARS-CoV-2, diagnostics, treatment, and clinical outcomes in solid organ transplant recipients as well as transplant activity during the COVID-19 pandemic.

- Systematic review including 215 studies and 2772 solid organ transplant recipients (and meta-analysis including 60 studies) evaluating treatment strategies and outcomes related to SARS-CoV-2 infection.


- Review of data for SARS-CoV-2 vaccines in solid organ transplant recipients including humoral and cellular immune response and proposed alternative immunization schemes.

- Review of immune response to SARS-CoV-2 infection in solid organ transplant recipients, including some comparisons to non-transplant patients.

- Systematic review and meta-analysis including 202 solid organ transplant recipients evaluating maintenance immunosuppression strategies in the setting of COVID-19 disease.

- Randomized, placebo-controlled trial for a third dose of mRNA-1273 vaccine in solid organ transplant recipients. Patients receiving a third dose had significantly higher immunogenicity than those receiving placebo.

- This case report summarizes perioperative presentation to aid clinicians in identifying potential COVID-19 cases in patients prior to transplantation.

- A summarization of collective viewpoints on the emerging COVID-19 pandemic, including mitigation strategies and impact on organ transplantation.

- This case report describes an atypical intial presentation of novel COVID-19 in a solid organ transplant recipient.

- American Society of Transplantations’s guidelines on RNA respiratory viral infections in solid organ transplant recipients


- Retrospective cohort analysis of adult patients diagnosed with RSV infection and treated with ribavirin


- Randomized, double-blind trial comparing the safety and immunogenicity of the 2016-2017 high dose vs standard dose influenza vaccine in adult transplant recipients


- Series of 56 episodes of RSV are described to evaluate the efficacy, safety, and cost-effectiveness of oral ribavirin for the treatment of RSV infection after lung transplant


- Analysis of 9 lung transplant recipients treated with oseltamivir for influenza infection


- Retrospective study investigating outcomes of oral versus inhaled ribavirin therapy


- Review article describing influenza vaccines in transplant recipients


- Review of the literature examining viral respiratory infections in lung transplant recipients and their effect on graft complications


- Multicenter cohort study of adults and children who received organ transplants with confirmation of influenza A infection to assess morbidity and mortality


- Use of oral ribavirin in five lung transplant recipients with RSV is described

- The mainstay of treatment of human metapneumovirus consist of intravenous ribavirin at a starting dose of 33 mg/kg/day for the first 24 hours, then 20 mg/kg/day thereafter. Duration of therapy was determined by resolution of clinical symptoms and sustained improvements in respiratory function.


- A multicenter prospective trial on hematopoietic cell transplant recipients with respiratory syncytial virus infection of the upper airways investigates the safety and efficacy of aerosolized ribavirin in preventing disease progression.


- A study that investigated the utility of intravenous (IV) ribavirin with steroids for the treatment of RSV infection after LTx. In 18 symptomatic patients.


- Review article describing parainfluenza virus infection in adult lung transplant recipients.

7.1.11 Measles


- Broad-spectrum anti-infective drugs combined with IVIG should be given for Measles infection in pediatric liver transplant recipients.


- This report summarizes exposure to measles through international travel and illustrates the potential for immunocompromised patients to encounter the virus despite common coverage with effective vaccine in the US.


- A review of published data on the efficacy and safety of live viral vaccines for measles, mumps, rubella, or varicella in post-transplant patients currently on immunosuppression.

- Serologies of 18 children were reviewed 6 months post-transplant. Four of 18 (22.2%) and 2/18 (11.1%) lost immunity to measles and varicella, respectively.

7.2 Bacterial

7.2.1 Central venous catheter infections and treatment options

- Review of Candida related in vitro, in vivo data, and case studies related to antifungal lock therapy


- Updated guidelines for management of CVC infections, including recommended antibiotic therapies with duration for catheter-related infections


- Cochrane review of 30 studies comparing antimicrobial (antibiotic and non-antibiotic) lock solutions to standard sealing solutions (usually heparin) of the CVC for HD. Authors concluded that antibiotic antimicrobial and combined (antibiotic-non antibiotic) lock solutions decreased infections compared to control lock solutions, whereas non-antibiotic lock solutions reduced infections only for tunnelled CVC. The level of confidence of the conclusions is low.


- Guidelines for management of CVC infections, including recommended antibiotic therapies for specific pathogens.


- IDSA guidelines for prevention of catheter-related infections.

- Recommendations for management of catheter-related bloodstream infections in heart transplant patients. Recommends empiric coverage of Gram-positive and Gram-negative bacteria as well as Candida spp., and antimicrobial therapy for durations longer than would be used in other patients.


- Observational study in stem cell transplant patients showed a significant decrease in rates of catheter-related bloodstream infections after switching from isopropanol to chlorhexidine for disinfection of catheter connections.


- Prospective non-randomized study of antimicrobial-coated CVCs (n= 58) compared with uncoated (n= 49) uncoated CVCs. Significantly fewer fever days per 1,000 catheter days and positive blood cultures were observed in the antimicrobial covered CVC group.

7.2.2 Mycobacterium tuberculosis

- Review of OPTN reports of donor derived tuberculosis to evaluate outcomes and better understand donor derived tuberculosis


- Review of current approaches to diagnosis and treatment options of latent TB infections (LTBI) and TB disease in solid organ transplant donors and recipients


- AST IDCOP 2019 Guidelines on Mycobacterium Tuberculosis in Solid Organ Transplantation

- Literature review of cohort and RCTs regarding treatment agents for latent TB infections in SOT patients


- RCT illustrating 12 weeks of RPT/INH as an alternative to 9 months of INH for latent TB


- IDSA guidelines for drug susceptible TB


  - Retrospective, observational study that attempted to identify risk factors for immune reconstitution syndrome in transplants patients being treated for TB.


  - Consensus report on the potential for donor derived TB and how to manage recipients with potential donor exposure.


  - A literature review on the use of TB prophylaxis in kidney transplant recipients


  - Consensus statement that defines indications for treatment of latent TB in solid organ transplant recipients. This document also provides guidance in the treatment duration for TB in transplant recipients and how to manage drug interactions with immunosuppressive medications.


  - Multicenter study that identified the incidence and risk factors for developing TB in solid organ transplant recipients.
7.2.3 Nontuberculosis Mycobacterium


- Single-center, retrospective review of tedizolid and linezolid for the treatment of nontuberculous mycobacteria infections demonstrating a potential benefit in symptoms and microbiological improvement without significant adverse events


- AST IDCOP 2019 Update of Management of non-TB mycobacterium


- Retrospective review of non-tuberculous mycobacteria impact on lung transplant survival and chronic lung allograft dysfunction.


- Data to support use of inhaled amikacin in refractory cases


- IDSA guideline, update in progress as of 2018.


- Review of literature summarizing case reports of NTM infections in stem cell and solid organ transplant recipients.


- Review of mycobacterial species causing lung infection, epidemiology of infection, recommended treatment options.

- Review of 19 cases of NTM infection in renal transplant patients including treatment and outcomes.


- Retrospective study of 27 cases of mycobacterial infection after renal transplant of total of 1261 transplants. Seven patients were found to have infection with NTM organism. The article include description of clinical manifestations, treatment and outcomes.

### 7.2.4 Nocardia


- Case report of a kidney transplant recipient with cutaneous and pulmonary nocardiosis, treated with high-dose trimethoprim/sulfamethoxazole and linezolid in combination with reduced immunosuppression.


- A retrospective cohort study evaluating Nocardia recurrence in solid organ transplant recipients, specifically with forms of secondary prophylaxis.


- Case-control study of nocardia after lung transplant in 586 recipients assessing incidence, risk factors, efficacy of trimethoprim/sulfamethoxazole prophylaxis


- AST IDCOP 2019 update for Nocardia


- Epidemiologic and outcome data describing Nocardia infections in SOT and HCT recipients.

- Case-control study which identified 5 risk factors for nocardiosis after SOT which included a high calcineurin level in the month prior to diagnosis, use of tacrolimus at the time of diagnosis, corticosteroid dose at diagnosis, patient age, and length of stay in ICU after transplant.


- CLSI reporting standards for susceptibility of nocardia


- Ten-year retrospective evaluation of the epidemiology and identification of Nocardia isolates submitted to the CDC for antimicrobial susceptibility testing.


- Case control identifying risk factor for nocardiosis found recipient of high-dose steroids, history of CMV disease, and high levels of CNi as risk factor for nocardia in organ transplant recipients.

7.3 Fungal

7.3.1 PJP


- A retrospective analysis of adult renal transplant recipients receiving PJP prophylaxis evaluating anemia as an adverse effect of dapsone-treated patients compared to a control group of atovaquone-treated patients. All patients receiving dapsone had normal G6PD function.
- Dapsone was associated with a significantly greater decrease in hemoglobin from baseline. Median time to nadir hemoglobin from dapsone initiation was 30.5 days.


- A review article discussing epidemiology, pathophysiology, diagnosis, prophylaxis, etc. of Pneumocystis jirovecii.

- A multicenter, retrospective study describing the incidence, reasons for, and outcomes of using alternative prophylactic agents (APA) for PJP. APA use was possibly unwarranted in many cases, increasing the risk for APA-related side effects or preventable opportunistic infections.


- A meta-analysis determining the pooled effect of potential risk factors on post-transplant PJP in solid organ transplant recipients. In addition to the risk factors discussed in the AST Infectious Diseases Community of Practice guidelines, this study identified that recipients with lymphopenia, BK virus infections, and rituximab exposure should be considered for PJP prophylaxis.


- Retrospective, single-center study of using low-dose trimethoprim/sulfamethoxazole (10mg/kg/day) for the treatment of pneumocystis jirovecii pneumonia in deceased donor kidney transplant recipients demonstrated reduced adverse events without compromising efficacy.


- Retrospective study of using second line PJP prophylaxis agents (dapsone, atovaquone and pentamidine) at two large transplant centers demonstrated that the use of these agents after SOT is less than previously reported but less efficacious, less safe and expensive agents.


- Case-control study of 3,941 kidney and kidney-pancreas transplant patients who received 6 months of PCP prophylaxis with sulfamethoxazole-trimethoprim. Rejection and CMV infection were found to be independently associated with PCP development after completion of prophylaxis.


- AST IDCOP 2019 Updates to Management of PCP


- Multicenter study looking at PCP incidence with acute rejection (AR) and CMV infection found to PCP mostly as a late-onset disease occurring after completing course of prophylaxis, particularly among pts w/ AR or CMV infection.


- A retrospective analysis evaluating atovaquone 1500mg daily (N=25) compared to trimethoprim-sulfamethoxazole single-strength daily (N=160) for preventing pneumocystis carinii pneumonia within one year following kidney transplantation. No cases of pneumocystis carinii pneumonia were seen in either study group.


- Retrospective review evaluating pneumocystis jirovecii pneumonia (PCP) occurrence in kidney (N=657), kidney/pancreas (N=44), liver (N=436), lung or heart/lung (N=104) transplant recipients receiving trimethoprim-sulfamethoxazole for PCP prophylaxis for 6 months in kidney/pancreas, 12 months in lung, and no prophylaxis in liver transplant recipients. The overall incidence of PCP was low with the highest frequency seen in lung transplant recipients and all episodes occurring more than two years following transplant.


- Retrospective review evaluating pneumocystis jirovecii pneumonia (PCP) and Nocardia occurrence in 1352 kidney transplant recipients receiving trimethoprim-sulfamethoxazole prophylaxis for one month following transplant. The incidence of PCP and Nocardia was low in this patient population.


- Multicenter, open-label trial that evaluated atovaquone daily (N=536) compared to dapsone daily (N=521) as prophylaxis for the development of pneumocystis carinii pneumonia in human immunodeficiency virus positive patients who were intolerant to sulfamethoxazole-trimethoprim. The incidence of pneumocystis carinii pneumonia was similar among both study groups.

- Thirty-five clinical trials including those that compared prophylactic regimens to placebo, different doses of prophylactic agents, and different prophylactic regimens were analyzed to identify ideal medications and their respective doses to prevent pneumocystis carinii pneumonia.


- A retrospective analysis evaluating clindamycin/primaquine, trimethoprim-sulfamethoxazole, and dapsone prophylaxis for preventing pneumocystis carinii pneumonia in 206 patients with advanced human immunodeficiency virus infection. The rate of pneumocystis carinii pneumonia was lowest in patients receiving trimethoprim-sulfamethoxazole, followed by dapsone, then clindamycin/primaquine.


- Retrospective chart review that compared the efficacy of Bactrim, dapsone, and inhaled pentamidine for PCP prophylaxis in 200 HIV patients.


- Systematic review on the use of adjunctive corticosteroid therapy in AIDS patients with PCP pneumonia. Identified that steroid therapy was most beneficial in patients with arterial O2 pressures < 70 mmHg, alveolar arterial gradient > 35 mmHg on room air, and when started with 72 hr of PCP treatment.

7.3.2 Aspergillus

- Review article of article of aspergillus infections, including: immune response, risk factors, epidemiology, diagnosis, prophylaxis, treatment, resistance, etc.


- A retrospective review of liver transplant recipients who were colonized with Aspergillus pre-transplantation. It was concluded that prior colonization should not withhold or delay liver transplantation for otherwise acceptable candidates and can be managed with appropriate antifungal prophylaxis.

ECMM guidelines on mycological infections


- Single-center study describing experience with posaconazole, including dosing, plasma trough concentrations, safety, and tolerability with observations showing that DRT and IV formulations are both safe and effective in immunocompromised children, adolescents, and young adults. Higher dosing per body weight of DRT and IV Posaconazole may be required in patients < 13 years of age compared with patients 13 years of age and older to achieve therapeutic plasma concentrations.


- Review of diagnosis, prophylaxis, treatment, and assessment of response in invasive aspergillosis in solid organ transplant patients


- AST IDCOP 2019 updates for aspergillosis


- European guidelines for the managements of Aspergillus. Comments on various aspergillus strains, resistance, combination therapy, and TDM.


- IDSA guidelines for aspergillosis


- Non-inferiority trial comparing the efficacy of isavuconazole to voriconazole for the treatment of invasive mold infections. Majority of the study population had hematological malignancies and
had infections caused by Aspergillus. Isavuconazole was found to be non-inferior to voriconazole for the treatment of invasive mould infections and was associated with decreased adverse effects. However, therapeutic drug monitoring for voriconazole was not utilized.


- Randomized trial in patients with hematological malignancies with invasive aspergillosis infections treatment with voriconazole monotherapy or combination therapy with voriconazole and anidulafungin. Combination antifungal therapy was found to have a survival benefit compared to monotherapy, but this trial was not powered to make superiority claims.


- Study looking at use of oral vs IV use of voriconazole for treatment and found the need for higher oral than IV doses.


- Meta-analysis to determine the accuracy of serum galactomannan assays for diagnosing aspergillosis infections in immunocompromised patients. For solid organ transplant recipients, galactomannan assays were found to have a sensitivity of 0.22 and specificity of 0.84.


- Retrospective, case control series that identified risk factors for developing aspergillosis infections in solid organ transplant recipients. Risk factors included use of vasoactive agents, prolonged ICU stay post-transplant, renal failure requiring HD, CMV disease, or one episode of bacterial infection.


- A prospective, randomized trial comparing amphotericin B lipid complex and amphotericin B deoxycholate inhalations for prophylaxis of aspergillosis in lung transplant recipients. Both agents were associated with low rates of invasive fungal infections, but the lipid formulation was associated with decreased adverse effects.

- A retrospective study that aimed to characterize Aspergillus infections in lung transplant recipients. Patients that are pre-colonized with Aspergillus infections prior to lung transplant may benefit from systemic antifungal prophylaxis after transplant.


- RCT of voriconazole vs amphotericin which established voriconazole as a first-line agent for the treatment of aspergillosis with improved response and survival rates. TDM not used for voriconazole.

### 7.3.3 Cryptococcus


- Case report of an organ transplant-associated outbreak of C. gattii infection involving an HIV-negative immunosuppressed donor. 2 of the 3 recipients from this donor developed severe C. gattii infections following transplantation.


- AST IDCOP 2019 updates for cryptococcosis


- Two case reports of cryptococcosis infection early after liver transplantation, and review of literature in SOT.


- Treatment guidelines for cryptococcal disease in HIV-infected individuals, organ transplant recipients, and non-HIV-infected nontransplant hosts. Includes recommendations for other unique populations and those with Cryptococcus gattii infection.

- In 79 patients with central nervous system cryptococcosis, lipid formulations of amphotericin B were associated with lower mortality when compared to amphotericin B deoxycholate.


- Prospective, cohort study of patients with C. neoformans showed that lack of flucytosine induction is an independent risk factor for mycotic failure at two weeks.

### 7.3.4 Invasive Candidiasis


- A retrospective analysis of lung transplant recipients evaluating the effectiveness of perioperative anidulafungin for early invasive candidiasis prevention in addition to long-term triazole antifungal prophylaxis alone. There was no statistically significant difference in incidence of invasive candidiasis between cohorts (6% vs 13%, p=0.16).


- Pharmacokinetic study of fluconazole dosing for the prevention and treatment of invasive candidiasis in critically ill patients including solid organ transplant recipients


- Review of USRDS data to identify risk factors for invasive fungal infections (Candida, Histoplasmosis, Aspergillosis, cryptococcosis, other mycoses) in kidney transplant recipients. Identified risk factors include age > 65 years, diabetes, bacterial pneumonia and UTI.


- Non-inferiority of isavuconazole to caspofungin was not shown

- AST IDCOP 2019 updates to management of candida in SOT


- Updated review on Candida auris


- Retrospective review of liver transplant recipients to assess the feasibility and efficacy of tiered, targeted fungal prophylaxis. Intra-abdominal candidiasis was the most common fungal infection (73%); invasive fungal infections occurred in 6% of high-risk transplants who received prophylaxis versus 4% in low risk transplant who did not receive prophylaxis.


- Review of risk factors, prevention, diagnosis, and treatment of invasive fungal infections in SOT recipients (focus on candidiasis and aspergillosis).


- The American Society of Transplantation guidelines for management of donor-derived fungal infections in solid organ transplant recipients.


- Anidulafungin was non-inferior to fluconazole with a favorable response in the anidulafungin arm.


- Caspofungin was as effective as amphotericin B who had candidemia with a favorable response in the caspofungin arm.

7.3.5 Histoplasmosis

- AST IDCOP 2019 updates on managements of endemic fungal infections


- "VITAL" study: Open-label nonrandomized phase 3 trial evaluating efficacy and safety of isavuconazole in treatment of rare invasive fungal diseases. Seven of the patients were treated for histoplasmosis, with 1 having complete success, 3 with partial success, 1 with stable disease, and 2 with progression of disease. Median isavuconazole levels ranged from 3.2 ng/mL to 4.01 ng/mL and it was overall well tolerated.


- Review of the epidemiology, clinical presentation, and treatment strategies for Histoplasmosis and Blastomycosis in SOT recipients.


- Prospective surveillance study of 70 patients (64 SOT recipients) across 15 centers to characterize endemic infections in these patients.


- Retrospective review of 152 cases of histoplasmosis across 24 centers to identify risk factors and characterize infections. The average time to onset was 27 months, with the first year being the highest risk time frame. Ten percent of patients died, usually within the first month. In patients that survived one month after diagnosis, amphotericin followed by 12 months of an azole was usually successful.


7.4 Other

7.4.1 Timing of post-transplant infections (including donor-derived infections)

• AST IDCOP 2019 Guidelines on donor-derived infections


• Review of risk factors contributing to infections in transplant patients and timing of infections post-transplant.


• This article examines risk factors that contribute to infections in transplant patients as well as the timing of infections post-transplant.


• This review article presents a timeline for infections post-transplant.


• This is a review article that addresses patterns of infections post-transplant and the management of transplantation associated infections.


• This article provides definitions for infections in transplant patients to be used during clinical trials assessing immunosuppressive therapy and also provides recommendations for monitoring for infections.

• This is a review article focusing on the epidemiology of infections after transplant categorized into three time frames- the first month, second through sixth month, and greater than six months.


• Retrospective review analyzing the transmission rates and 30-day graft and patient survival outcomes for recipients of organs procured from bacteremic donors.

7.4.2 Infectious exposure management

7.4.2.1 Measles


• A review of the implementation of a systematic risk assessment during a large measles outbreak in the New York City area, with a total of 649 cases reported from 2018-2019.


• A retrospective study of kidney transplant patients to investigate the number of recipients who were evaluated for serologic status again MMR and varicella. It was found that the screening rate for MMR serologies was lower than varicella and pre-transplant infectious disease consult increased vaccination rate.


• The systematic risk assessment approach to identify and protect at-risk solid organ transplant recipients during the large measles outbreak in late 2018-summer of 2019 in the New York City area.


• This report summarizes exposure to measles through international travel and illustrates the potential for immunocompromised patients to encounter the virus despite common coverage with effective vaccine in the US.

Serologies of 18 children were reviewed 6 months post-transplant. Four of 18 (22.2%) and 2/18 (11.1%) lost immunity to measles and varicella, respectively.

7.4.2.2 Varicella

- Case report of a female child received live attenuated varicella vaccine 30 months after a living donor liver transplant at the age of 2 months. 2 year later however the antibody titer decreased to undetectable levels.


- Low-risk CMV solid organ transplant recipients receiving once-daily famciclovir experienced no HSV/VZV/CMV infection while on prophylaxis for a duration of 3 months.


- Case report of a 4-year-old boy who received the live attenuated MMR-varicella vaccine 16 months after receiving a living donor kidney transplant. He developed documented a disseminated varicella infection 5 weeks later.


- Review article on the management of varicella zoster in solid organ transplant recipients.


- No differences in median time to full healing of HSV rash were detected among patients receiving valacyclovir 1 gram TID versus 2 grams TID.


- Famciclovir 500 mg three times a day was compared to acyclovir 800 mg five times a day and no significant differences in new lesion formation, time to healing or duration of pain were observed.

• Acyclovir limited cutaneous dissemination as well as abbreviated duration of positive cultures, pain associated with lesions, postulation of lesions, crusting of lesions and complete healing of lesions.

7.4.2.3 Influenza


• Description of infection control and oseltamivir prophylaxis in an outbreak of 12 patients in a group of immunocompromised patients.

7.4.2.4 Tuberculosis


• CDC guidelines for evaluating patients at risk for developing TB after an exposure. Includes a section specifically regarding immunocompromised hosts that suggests considering them as “high priority” when evaluating potential contacts of a TB infected person.

7.4.2.5 Bacterial meningitis


• Guidelines for management of meningococcal outbreaks. There are no specific recommendations for immunocompromised patients.

7.4.3 Immunizations


• AST IDCOP 2019 updates on vaccinations


• AST ICDOP 2019 updates on travel medicine

• Refer to most recent CDC ACIP Immunization Schedule

• A column for immunocompromised conditions and recommended vaccinations can be found

- Initial studies on use of Shingrix in transplant recipients, additional trials currently underway.


- RCT which demonstrated that high dose vaccine may improve immunogenicity, study did not look at rates of disease.


- Booster dose 5 weeks after initial flu vaccination induces an increased antibody response.


- Recommendations 88 through 104 pertain to vaccination pre/post solid organ transplant. Contains references to the individually relevant trials in this area of study and highlights where recommendations vary from CDC guidelines.

### 7.4.4 Toxoplasmosis prophylaxis and treatment


- A retrospective review of SOT and HSCT recipients with toxoplasmosis between 2002 and 2018 at two large transplant centers in the United States.


- Case series of 3 patients (two liver, one lung) who developed post-transplant donor-derived toxoplasmosis. All patients were not on TMP-SMX prophylaxis at diagnosis, and two patients died with disseminated infection.

- American Society of Transplantation’s guidelines on the diagnosis, prevention, and management of toxoplasmosis in the pre- and post-transplant period


- Single center study of the effect of T. gondii donor and recipient serostatus on heart transplant outcomes including 5 year mortality and rates of CAV comparing results to previous studies of association of toxoplasmosis serostatus to outcomes.


- Multicenter study of cases of toxoplasmosis with details including diagnosis, manifestations and outcomes.


- Review article discussing the relative risk of toxoplasmosis infection, timing of infection and prophylaxis options in solid organ and hematopoietic stem cell transplant recipients.


- Summary of literature discussing chemoprophylaxis of toxoplasmosis infection.