7. Post-transplant infectious disease considerations

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7.1 Viral

7.1.1 Cytomegalovirus

Singh N, et al (2020). Effect of Preemptive Therapy vs Antiviral Prophylaxis on Cytomegalovirus Disease in Seronegative Liver Transplant Recipients with Seropositive Donors. JAMA; 323(14):1378-1387. Retrieved from: https://jamanetwork.com/journals/jama/article-abstract/2764457

- 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.

Laub MR et al, (2020). Delayed versus initial cytomegalovirus prophylaxis after kidney transplantation. Clin Transplant. doi: 10.1111/ctr.13854 [Epub ahead of print]. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/32163619

- 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.

Phoompoung P, et al (2019). Letermovir as salvage therapy for cytomegalovirus infection in transplant recipients. Transplantation;104;404-409. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/31107821

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

Turner N, Strand A, Grewal DS, et al (2019). Use of letermovir as salvage therapy for drug-resistant cytomegalovirus. Antimicrob Agents Chemother. 63(3):e02337-18. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/30642941

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

Westall G, et al. (2019). A Randomized Study of Quantiferon CMV-directed Versus Fixed-duration Valganciclovir Prophylaxis to Reduce Late CMV After Lung Transplantation. Transplantation;103(5):1005-13. Retrieved at https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/30247316

- 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

Maertens J, et al (2019). Maribavir for Preemptive Treatment of Cytomegalovirus Reactivation. N Engl J Med; 381(12):1136-47. Retrieved at https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/31532960

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

Kotton CN et al (2018). The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-Organ Transplantation. Transplantation;102:900-931. Retrieved from:

https://journals.lww.com/transplantjournal/fulltext/2018/06000/The_Third_International_Consensus_Guidelines_on.13.aspx

- 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

Vincenti F, et al (2018). A randomized, phase 2 study of ASP0113, a DNA-based vaccine, for the prevention of CMV in CMV-seronegative kidney transplant recipients receiving a kidney from a CMV-seropositive donor. Am J Transplant. 18(12):2945-54. Retrieved from: https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29745007

- 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

Witzke O et al (2018). Valganciclovir prophylaxis versus preemptive therapy in cytomegalovirus-positive renal allograft recipients: long-term results after 7 years of a randomized clinical trial. Transplantation; 102(5):876-82. Retrieved at https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29166336

- 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

Hensler et al, (2018). Impact of electronic health record-based, pharmacist-driven valganciclovir dose optimization in solid organ transplant recipients. Transplant Infectious Diseases. Epublication ahead of print retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/29360250

- 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.

Bruminhent J et al, (2017). Epidemiology and outcome of ganciclovir-resistant cytomegalovirus infection after solid organ transplantation: a single transplant center experience in Thailand. Transplant Proceedings. 49(5):1048-1052. https://www.ncbi.nlm.nih.gov/pubmed/28369203

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

Marty F, et al (2017). Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic-Cell Transplantation. N Engl J Med; 377(25):2433-2444. Retrieved at https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29211658

- 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 pilot study. Transpl Infect Dis;19(6). Retrieved at https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/28921781

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

Camara R et al, (2016). CMV in Hematopoietic Stem Cell Transplantation. Mediterranean journal of hematology and infectious diseases. 8(1): e2016031. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928522/

- 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.

Limaye AP et al, (2016). Plasma IL-10 Levels to Guide Antiviral Prophylaxis Prevention of Late-Onset Cytomegalovirus Disease, in High Risk Solid Kidney and Liver Transplant Recipients. Transplantation,100(1):210-6. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26680375

- 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

Bradley D, et al. (2016). Pharmacokinetics and Safety of Valganciclovir in Pediatric Heart Transplant Recipients 4 Months of Age and Younger. Pediatr Infect Dis J, 35(12):1324-1328. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/27580058

- 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.

Durante-Mangoni E, et al. (2015). Effect of the immunosuppressive regimen on the incidence of cytomegalovirus infection in 378 heart transplant recipients: A single centre, prospective cohort study. J Clin Virol, 68:37-42. Retrieved at: https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+the+immunosuppressive+regimen+on+the+incidence+of+cytomegalovirus+infection+in+378+heart+transplant+recipients%3A+A+single+centre%2C+prospective+cohort+study.

- 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 Transplantation Society guidelines (2015). The Prevention and Management of CMV Disease after Solid Organ Transplantation. Third edition. Retrieved from https://bts.org.uk/wp-content/uploads/2016/09/14_BTS_CMV_3RDE-1.pdf

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

Cowan J et al, (2015). Protocol for updating a systematic review of randomized controlled trials on the prophylactic use of intravenous immunoglobulin for patients undergoing hematopoietic stem cell transplantation.BMJ open 5(8):e008316. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26297369

- 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

Requião-Moura LR et al, (2015). Cytomegalovirus infection in renal transplantation: clinical aspects, management and the perspectives. Einstein (Sao Paulo), 13(1):142-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25993081

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

Gabardi, S et al, (2015). Evaluation of low-versus high-dose Valganciclovir for prevention of cytomegalovirus disease in high-risk renal transplant recipients. Transplantation. 99(7), 1499-1505.Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25643140

- 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

Ramanan P et al, (2013).Cytomegalovirus Infections in Solid Organ Transplantation: A Review. Infection & chemotherapy. 45(3): 260–271. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3848521/

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

RazonableR, Humar A; AST Infectious Diseases Community of Practice. (2013). Cytomegalovirus in solid organ transplant recipients. Am J Transplant. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/23465003

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

Stoelben S et al (2013). Preemptive treatment of cytomegalovirus infection in kidney transplant recipients with letermovir: results of a phase 2a study. Transplant International. 27:77-86. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Preemptive+treatment+of+Cytomegalovirus+infection+in+kidney+transplant+recipients+with+letermovir%3A+results+of+a+Phase+2a+study

- 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.

Witzke O et al. (2012). Valganciclovir prophylaxis versus preemptive therapy in cytomegalovirus-positive renal allograft recipients: 1-year results of a randomized clinical trial. Transplantation, 93(1), 61-8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22094954

- 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.

Andre C. Kalil et al, (2011). Effectiveness of Valganciclovir 900 mg versus 450 mg for Cytomegalovirus Prophylaxis in Transplantation: Direct and Indirect Treatment Comparison Meta-analysis. Clinical Infectious Diseases. 52(3):313-321. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/21189424

- 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

Finlen Copeland CA et al, (2011). Long-term efficacy and safety of 12 months of valganciclovir prophylaxis compared with 3 months after lung transplantation: A single-center, long-term follow-up analysis from a randomized, controlled cytomegalovirus prevention trial. The Journal of heart and lung transplantation. 30(9):990-6. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/21489817

- 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

Palmer SM et al. (2010). Extended valganciclovir prophylaxis to prevent cytomegalovirus after lung transplantation: A randomized, controlled trial. Annals of internal medicine. 152(12):761-9. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/20547904

- 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

Humar A et al, (2010). The efficacy and safety of 200 days valganciclovir cytomegalovirus prophylaxis in high-risk kidney transplant recipients. Am J of Transplant, 10(5), 1228-37. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20353469

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

Humar A et al, (2010). Extended valganciclovir prophylaxis in D+/R- kidney transplant recipients is associated with long-term reduction in cytomegalovirus disease: two-year results of the IMPACT study. Transplantation. 90(12):1427-31. Retrieved at: https://www.ncbi.nlm.nih.gov/pubmed/21197713

- 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

Avery RK et al, (2010). Utility of leflunomide in the treatment of complex cytomegalovirus syndromes. Transplantation. 90(4):419-26. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/20683281

- 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

Asberg A et al, (2009). Long-term outcomes of CMV disease treatment with valganciclovir versus IV ganciclovir in solid organ transplant recipients. American journal of transplantation. 9(5):1205-13. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/19422345

- 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

Bonaros N et al. (2008). CMV-hyperimmune globulin for preventing cytomegalovirus infection and disease in solid organ transplant recipients: a meta-analysis. Clinical Transplantation, 22(1), 89-97. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18217909

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

Reischig T et al. (2008). Valacyclovir prophylaxis versus preemptive valganciclovir therapy to prevent cytomegalovirus disease after renal transplantation. American Journal of Transplantation, 8(1), 69-77. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17973956

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

Asberg A et al, (2007). Oral valganciclovir is noninferior to intravenous ganciclovir for the treatment of cytomegalovirus disease in solid organ transplant recipients. American journal of transplantation. 7(9):2106-13.Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/17640310

- 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.

Small LN, et al. (2006). Preventing post-organ transplantation cytomegalovirus disease with ganciclovir: a meta-analysis comparing prophylactic and preemptive therapies. Clinical infectious diseases, 43(7), 869-80. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16941368

- 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.

Khoury JA et al. (2006). Prophylactic versus preemptive oral valganciclovir for the management of cytomegalovirus infection in adult renal transplant recipients. American Journal of Transplantation, 6(9), 2134-43. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16780548

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

Ehlert K et al, (2006). Treatment of refractory CMV-infection following hematopoietic stem cell transplantation with the combination of foscarnet and leflunomide. Klinische Pädiatrie 218(3):180-4. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16688677

- 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

Paya C et al, (2004). Efficacy and safety of valganciclovir vs. oral ganciclovir for prevention of cytomegalovirus disease in solid organ transplant recipients. American journal of transplantation. 4(4):611-20. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/15023154

- 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- o-onset of CMV disease and to viremia was compared.

Zamora MR et al, (2004). Following universal prophylaxis with intravenous ganciclovir and cytomegalovirus immune globulin, valganciclovir is safe and effective for prevention of CMV infection following lung transplantation. Am J Transplant. 4: 1635–1642. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/15367218

- 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

Lowance D et al. (1999). Valacyclovir for the prevention of cytomegalovirus disease after renal transplantation. International Valacyclovir Cytomegalovirus Prophylaxis Transplantation Study Group. N Engl J Med, 340(19), 1462-70. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10320384

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

7.1.2 Epstein-Barr Virus and Lymphoproliferative disorder

Allen U, et al (2019). Post-transplant lymphoproliferative disorders, Epstein-Barr virus infection, and disease in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;33e13652. Available at https://doi.org/10.1111/ctr.13652

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

Dierickx D,Habermann TM. Post-transplantation lymphoproliferative disorders in adults (2018). N Engl J Med. 378:549-62. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMra1702693

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

Pagano J, et al. Antiviral Drugs for EBV (2018). Cancers;10(6):197. Retrieved from https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29899236

- Review article describing antiviral drugs used to inhibit EBV replication

Al Dabbagh MA, et al (2017). The role of antiviral prophylaxis for the prevention of Epstein-Barr virus associated posttransplant lymphoproliferative disease in solid organ transplant recipients: a systematic review. Am J Transplant.17(3):770-781. Retrieved from https://www-ncbi-nlm-nih-gov.ezproxy2.umc.edu/pubmed/27545492

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

Yager J, et al. (2017). Valganciclovir for the Suppression of Epstein-Barr Virus Replication. J Infect Dis;216(2):198-202. doi: 10.1093/infdis/jix263.

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

Styczynski J et al, (2016). Management of Epstein-Barr Virus infections and post-transplant lymphoproliferative disorders in patients after allogeneic hematopoietic stem cell transplantation: Sixth European Conference on Infections in Leukemia (ECIL-6) guidelines. Haematologica. 101(7):803-11. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27365460

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

Mumtaz K et al, (2015). Post-transplant lymphoproliferative disorder in liver recipients: Characteristics, management, and outcome from a single-center experience with >1000 liver transplantations. Canadian journal of gastroenterology & hepatology. 29(8):417-22 Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26076399

- 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.

Evens AM et al, (2010). A multicenter analysis of 80 solid organ transplantation recipients with post transplantation lymphoproliferative disease: outcomes and prognostic factors in the modern era. Journal of clinical oncology. 28(6):1038-46. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/20085936

- 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.

Opelz G et al, (2007). Effect of cytomegalovirus prophylaxis with immunoglobulin or with antiviral drugs on post-transplantation-Hodgkin lymphoma: a multicentre retrospective analysis. The Lancet Oncology. 8(3):212-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/17329191

- 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

Humar A et al, (2006). A randomized trial of ganciclovir versus ganciclovir plus immune globulin for prophylaxis against Epstein-Barr virus related posttransplant lymphoproliferative disorder. Transplantation. 81(6):856-61. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16570008

- 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

Green M et al, (2006). CMV-IVIG for prevention of Epstein Barr virus disease and posttransplant lymphoproliferative disease in pediatric liver transplant recipients. American Journal of Transplantation. 6(8):1906-12. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16889546

- A randomized controlled trial of 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

Vink P, et al (2020). Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in chronically immunosuppressed adults following renal transplant: a phase III, randomized clinical trial. Clin Infect Dis;70(2):181-190. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/30843046

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

Lee D, et al. (2019). Herpes simplex virus infections in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;e13526. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/30859647

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

Pergam S, et al. (2019). Varicella zoster virus in solid organ transplantation. Am J Transplant; Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/23465007

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

Lindahl J, et al (2018) Long-term study showed that vaccination protected pediatric renal transplant recipients from life-threatening varicella zoster virus. Acta Paediatr;107:2185-92. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/29706010.

- 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

Macesic N et al (2017). Herpes simplex virus-2 transmission following solid organ transplantation: donor-derived infection and transplantation from prior organ recipients. Transplant Infectious Disease. 19 (5):1-8. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/28618165

- 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.

Styczynsk, J et al,(2009). Management of HSV, VZV and EBV infections in patients with hematological malignancies and after SCT: guidelines from the Second European Conference on Infections in Leukemia. Bone marrow transplantation, 43(10), 757-770. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19043458

- 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. Journal of Infectious Diseases, 197, 1289-1295. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18422441

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

Boeckh M et al, (2006) Long-term acyclovir for prevention of varicella zoster virus disease after allogeneic hematopoietic cell transplantation—a randomized double-blind placebo-controlled study. Blood. 107(5):1800-5. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16282339

- 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

Fiddian P et al, (2002). Valacyclovir provides optimum acyclovir exposure for prevention of cytomegalovirus and related outcomes after organ transplantation. The Journal of infectious diseases. 186 Suppl 1:S110-5. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12353195

- 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)

Tyring S et al, (2001). Collaborative Famciclovir Immunocompromised Study Group. A randomized, double-blind trial of famciclovir versus acyclovir for the treatment of localized dermatomal herpes zoster in immunocompromised patients. Cancer Investigation, 19, 13-22. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11291551

- 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

Shepp DH et al, (1986). Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. New England Journal of Medicine, 314, 208-212. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3001523

- 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

Florescu D, et al. (2019). Adenovirus in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;33e13527. https://doi.org/10.1111/ctr.13527. doi: 10.1016/j.bbmt.2016.12.621.

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

Gonzalez-Vicent et al. (2019). Current practices in the management of adenovirus infection in allogeneic hematopoietic stem cell transplant recipients in Europe: The AdVance study. Eur J Haematol;102(3):210-217. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/30418684

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

Grimley M, et al. (2017) Brincidofovir for Asymptomatic Adenovirus Viremia in Pediatric and Adult Allogeneic Hematopoietic Cell Transplant Recipients: A Randomized Placebo-Controlled Phase II Trial. Biol Blood Marrow Transplant;23(3):512-21. Retrieved at https://www.ncbi.nlm.nih.gov/pubmed/28063938

- 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

Wy Ip W et al, (2013). Management of adenovirus in children after allogeneic hematopoietic stem cell transplantation. Advances in hematology. 176418. Epub 2013 Oct 28. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/24288536

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

7.1.5 HBV prophylaxis and treatment

Te H, et al. (2019). Viral hepatitis: Guidelines by the American Society of Transplantation Infectious Disease Community of Practice. Am J Transplant;33:e13514. https://doi.org/10.1111/ctr.13514

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

Wong T, et al (2019). Liver transplantation using Hepatitis B core positive grafts with antiviral monotherapy prophylaxis. J Hepatol;70(6):1114-1122. doi: 10.1016/j.jhep.2019.03.003

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

European Association for the Study of the Liver (2017). EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol;67(2):370-398. doi: 10.1016/j.jhep.2017.03.021

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

Choi H, et al. (2017) A multicenter phase III study to evaluate the efficacy and safety of Hepabulin, a new Hepatitis B Immunoglobulin, in liver transplantation recipients with Hepatitis B. Ann Transplant;22:740-748. Available at https://www.ncbi.nlm.nih.gov/pubmed/29229898

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

Malik M, et al. (2017). Prophylaxis among Hepatitis B core antibody-positive deceased-donor liver transplant recipients: Hepatitis B Immunoglobulin plus oral antiviral agents versus antiviral agents alone: a single-center experience. Exp Clin Transplant;15(2):183-188. doi: 10.6002/ect.2015.0277

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

Fung J, et al (2017). Long-term outcomes of entecavir monotherapy for chronic hepatitis B after liver transplantation: Results up to 8 years. Hepatology;66(4):1036-44. doi: 10.1002/hep.29191

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

Terrault, NA et al, (2016). AASLD guidelines for treatment of chronic hepatitis B. Hepatology, 63(1), 261-283. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26566064

- 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

Fernando B, Melisa D, (2016). Management of hepatitis B reactivation in immunosuppressed patients: An update on current recommendations. World journal of hepatology. 8(8): 385–394. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4794528/

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

Saab S et al, (2016). The Management of Hepatitis B in Liver Transplant Recipients. Clinics in liver disease. 20(4):721-736. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27742010

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

Jiménez-Pérez M et al, (2015). Management of hepatitis B virus infection after liver transplantation. World journal of gastroenterology. 21(42):12083-90. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26576093.

- 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.

Fung J, (2015). Management of chronic hepatitis B before and after liver transplantation. World journal of gastroenterology. 7(10):1421-6. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26052387

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

Yap DY et al, (2010). Long-term outcome of renal transplant recipients with chronic hepatitis B infection-impact of antiviral treatments. Transplantation, 90(3), 325-30. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20562676

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

Tse KC et al, (2010). Response to adefovir or entecavir in renal allograft recipients with hepatitis flare due to lamivudine-resistant hepatitis B. Clinical Transplantation, 24(2), 207-12. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19758269

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

Vallet-Pichard et al, (2011). Viral hepatitis in solid organ transplantation other than liver. Journal of hepatology, 55(2), 474-482.Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21241754

- 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

Idilman R Arat M, (2011). Evaluation and management of hepatitis B virus infection in hematopoietic stem cell transplantation: before and after transplantation. Expert review of anti-infective therapy. 9(8):641-52. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21819330

- 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.

Potthoff A et al, (2006). Improved outcome of chronic hepatitis B after heart transplantation by long-term antiviral therapy. Journal of Viral Hepatitis, 13(11), 734-41. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17052272

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

Perrillo R et al, (2004). Adefovir dipivoxil added to ongoing lamivudine in chronic hepatitis B with YMDD mutant hepatitis B virus. Gastroenterology, 126(1), 81-90. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14699490

- 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.

Buti M et al, (2003). A randomized study comparing lamivudine monotherapy after a short course of hepatitis B immune globulin (HBIg) and lamivudine with long-term lamivudine plus HBIg in the prevention of hepatitis B virus recurrence after liver transplantation. Journal of Hepatology, 38(6), 811-7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12763375

- 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.

Schiff ER et al, (2003). Adefovir dipivoxil therapy for lamivudine-resistant hepatitis B in pre- and post-liver transplantation patients. Hepatology, 38(6), 1419-27. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14647053

- 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

Gupta G, et al (2020). Ultra-short duration direct acting antiviral prophylaxis to prevent virus transmission from hepatitis C viremic donors to hepatitis C negative kidney transplant recipients. Am J Transplant;20(3):739-751. doi: 10.1111/ajt.15664.

- 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.

Woolley A et al (2019). Heart and lung transplants from HCV-infected donors to uninfected recipients. N Engl J Med;380(17):1606-1617. doi: 10.1056/NEJMoa1812406

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

Durand C et al (2018). Direct-acting antiviral prophylaxis in kidney transplantation from hepatitis c virus-infected donors to noninfected recipients. Ann Intern Med; 168(8):533-540. doi: 10.7326/M17-2871.

- 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 (2018). Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Retrieved from https://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/

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

American Association for the Study of Liver Diseases (2018). AASLD IDSA recommendations for testing, managing, and treating Hepatitis C virus infection;67(10):1477-92. doi: 10.1093/cid/ciy585

- 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

Belli L, et al. (2018). Impact of DAAs on liver transplantation: Major effects on the evolution of indications and results. An ELITA study based on the ELTR registry. J Hepatol;69(4):810-817. doi: 10.1016/j.jhep.2018.06.010

- 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

Recommendations for Testing, Managing, and Treating Hepatitis C. Retrieved Jan 2018, from http://www.hcvguidelines.org

- 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.

Bari K et al (2018). Hepatitis C transmission from seropositive, nonviremic donors to non-hepatitis C liver transplant recipients. Hepatology;67(5):1673-82. doi: 10.1002/hep.29704.

- 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

Schlendorf K et al (2018). Early outcomes using hepatitis C-positive donors for cardiac transplantation in the era of effective direct-acting anti-viral therapies. J Heart Lung Transplant;37(6):763-9. doi: 10.1016/j.healun.2018.01.1293

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

Reese P, et al (2018) Twelve-month outcomes after transplant of hepatitis c-infected kidneys into uninfected recipients: a single group trial. Ann Intern Med;169(5):273-281. doi: 10.7326/M18-074

- 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)

Goldberg D et al (2017) Trial of transplantation of HCV-infected kidneys into uninfected recipients. N Engl J Med;376(24):2394-2395. doi: 10.1056/NEJMc1705221

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

Levitsky J et al (2017). The American Society of Transplantation Consensus Conference on the use of Hepatitis C viremic donors in solid organ transplantation. Am J Transplantation. 17:2790-2802. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28556422

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

Irwin L et al (2017). Utilization of increased risk for transmission of infectious disease donor organs in solid organ transplantation: retrospective analysis of disease transmission and safety. Transplant Infectious Disease. 19(6): e12791.

- 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.

Bowring M et al (2017). Changes in utilization and discard of hepatitis c-infected donor livers in the recent era. Am J Transplant;17(2):519-527. doi: 10.1111/ajt.13976.

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

Forns X, et al, (2017). Efficacy, safety, and pharmacokinetics of simeprevir, daclatasvir, and ribavirin in patients with recurrent hepatitis C virus genotype 1b infection after orthotopic liver transplantation: The Phase II SATURN study. Transplan Infec Dis. 2017 Mar 13. doi: 10.1111/tid.12696. [Epub ahead of print] Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28295849

- 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.

Shoreibah M, et al, (2017). Ledipasvir/sofosbuvir without ribavirin is effective in the treatment of recurrent hepatitis C virus infection post-liver transplant. Hepatology International. 2017 Jan 12. doi: 10.1007/s12072-016-9778-6. [Epub ahead of print] Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28083718

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

Stepanova M, et al. (2016). Long-term outcomes of heart transplant recipients with hepatitis C positivity: the data from the U.S. transplant registry. Clin Transplant, 30(12):1570-1577. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/27739127

- 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.

Lubetzky M, et al (2016). Safety and Efficacy of Treatment of Hepatitis C in Kidney Transplant Recipients with Directly Acting Antiviral Agents. Transplantation. 2016 Dec 22. doi: 10.1097/TP.0000000000001618. [Epub ahead of print]. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/28009781

- 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.

Levitsky J et al (2016). Perioperative ledipasvir-sofosbuvir for HCV in liver-transplant recipients. N Engl J Med;375(21):2106-8. DOI: 10.1056/NEJMc1611829

- 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

Belga, S. et al, (2016). Hepatitis C in non-hepatic solid organ transplant candidates and recipients: A new horizon. World journal of gastroenterology, 22(4), 1650. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4721996/

- 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

Taylor J et al, (2016). Management of Post-Liver Transplant Recurrence of Hepatitis C. Drugs. [Epub ahead of print]. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27878476

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

Jothimani D et al, (2016). Management of post liver transplantation recurrent hepatitis C infection with directly acting antiviral drugs: a review. Hepatology international. 10(5):749-61. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27337961

- 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

Pillai AA et al, (2016). Simeprevir and Sofosbuvir (SMV-SOF) for 12 Weeks for the Treatment of Chronic Hepatitis C Genotype 1 Infection: A Real World (Transplant) Hepatology Practice Experience. The American journal of gastroenterology. 111(2):250-60. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26832650

- 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

Poordad F et al, (2016). Daclatasvir with sofosbuvir and ribavirin for hepatitis C virus infection with advanced cirrhosis or post-liver transplantation recurrence. Hepatology. 63(5):1493-505. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26754432

- 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

Fontana RJ et al, (2016). Daclatasvir combined with sofosbuvir or simeprevir in liver transplant recipients with severe recurrent Hepatitis C infection. *Liver Transplantation*. 22: 446-458. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26890629

- 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.

Brown RS et al, (2016). Interferon-free therapy for genotype 1 hepatitis C in liver transplant recipients: real world experience from the Hepatitis C therapeutic registry and Research network. *Liver Transplantation* . 22: 24-33. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26519873

- 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.

O'Leary JG et al, (2016). Efficacy and safety of simeprevir and sofosbuvir with and without ribavirin for 12 weeks in subjects with recurrent genotype 1 hepatitis C post-orthotopic liver transplant: The GALAXY study. (Abstract). *Journal of Hepatology*. 64: Suppl 2: S540. Retrieved from http://www.journal-of-hepatology.eu/article/S0168-8278(16)00962-4/abstract

- 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

Pungpapong S et al, (2015). Multicenter experience using simeprevir and sofosbuvir with or without ribavirin to treat hepatitis C genotype 1 after liver transplant. *Hepatology.* 2015 Jun;61(6):1880-6. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25722203

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

Punzalan CS et al, (2015). Sofosbuvir plus simeprevir treatment of recurrent genotype 1 hepatitis C after liver transplant. Clinical transplantation. 29(12):1105-11. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26358816

- 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.

Leroy V et al, (2015). Efficacy of Sofosbuvir and Daclatasvir in Patients With Fibrosing Cholestatic Hepatitis C After Liver Transplantation. Clinical gastroenterology and hepatology. 13(11):1993-2001. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26044317

- 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

Charlton M et al, (2015). Sofosbuvir and ribavirin for treatment of compensated recurrent hepatitis C virus infection after liver transplantation. Gastroenterology. 148(1):108-17. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25304641

- 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

Torres HA et al, (2015). Hepatitis C Virus Infection among Hematopoietic Cell Transplant Donors and Recipients: American Society for Blood and Marrow Transplantation Task Force Recommendations. Biology of blood and marrow transplantation. 21(11):1870-82. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26256943

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

Barsa JEet al, (2015). A pleasant dilemma to have: to treat the HCV patient on the waiting list or to treat post-liver transplantation?. Clinical transplantation. 29(10):859-65. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26329668

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

Curry MP et al, (2015). Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation: an open-label study. Gastroenterology. 148(1):100-107. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25261839

- 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

Charlton M et al, (2015). Ledipasvir and Sofosbuvir Plus Ribavirin for Treatment of HCV Infection in Patients With Advanced Liver Disease. *Gastroenterology*. 149(3):649-59. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25985734

- 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

Forns X et al, (2015). Sofosbuvir compassionate use program for patients with severe recurrent hepatitis C after liver transplantation. *Hepatology*. 61(5):1485-1494. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25557906

- 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.

Feld JJ et al, (2015). Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *N Engl J Med*. 373(27):2599-607. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26571066

- 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

Curry MP et al, (2015). Sofosbuvir and Velpatasvir for HCV in patients with Decompensated cirrhosis. *NEJM* . 27: 2618-2628. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26569658

- 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

Afdhal N, et al. (2014). Ledipasvir and sofosuvir for previously treated HCV genotype 1 infection. New England Journal of Medicine, 370(16), 1483-93. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24725238

- 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.

Kowdley KV, et al. (2014). Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. New England Journal of Medicine, 370(20), 1879-88. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24720702

- Prospective, randomized trial evaluating ledipasvir and sofosbuvir with or without ribavirin therapy 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.

Zeuzem S et al, (2014). Simeprevir increases rate of sustained virologic response among treatment-experienced patients with HCV genotype 1 infection: a phase IIb trial. Gastroenterology 146 (2), 430-441. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24184810

- 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.

Reddy KR et al, (2014). Ledipasvir/sofosbuvir with ribavirin for the treatment of HCV in patients with post transplant recurrence: preliminary results of a prospective, multicenter study. [Abstract 8.] 65th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). November 7-11, 2014; Boston, MA. Retrieved from http://liverlearning.aasld.org/aasld/2014/thelivermeeting/60057/[[$toc.link]]

- 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

Lawitz E et al, (2013). Sofosbuvir for previously untreated chronic hepatitis C infection. N Eng J Med, 368(20), 1878-87. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23607594

- 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.

Jacobson IM et al, (2013). Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl JMed, 368(20), 1867-77. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23607593

- 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)

Anesi J, et al (2019). Arenaviruses and West Nile Virus in solid organ transplant recipients. Am J Transplant;33(9):e13576. doi: 10.1111/ctr.13576

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

Yango, AF et al,(2014). West Nile virus infection in kidney and pancreas transplant recipients in the Dallas-Fort Worth Metroplex during the 2012 Texas epidemic. Transplantation, 97(9), 953-957. Retrieved from www.ncbi.nlm.nih.gov/pubmed/24406451

- 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

Winston, DJ et al, (2014). Donor-derived West Nile virus infection in solid organ transplant recipients: report of four additional cases and review of clinical, diagnostic, and therapeutic features. Transplantation, 97(9), 881-889. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/24827763.

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

Ravindra, KV et al, (2004). West Nile Virus—Associated Encephalitis in Recipients of Renal and Pancreas Transplants: Case Series and Literature Review. Clinical infectious diseases, 38(9), 1257-1260. Retrieved from www.ncbi.nlm.nih.gov/pubmed/15127337

- 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

Iwamoto M et al, (2003). Transmission of West Nile virus from an organ donor to four transplant recipients. New England Journal of Medicine, 348(22), 2196-2203. Retrieved from www.ncbi.nlm.nih.gov/pubmed/12773646

- 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

Hirsch et al. (2019). BK polyomavirus in solid organ transplantation – Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;e13528. https://doi.org/10.1111/ctr.13528

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

Patel S, et al (2019). Ciprofloxacin for BK viremia prophylaxis in kidney transplant recipients: Results of a prospective, double-blind, randomized, placebo-controlled trial. Am J Transplant;19(6):1831-1837. doi: 10.1111/ajt.15328

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

Bischof et al (2019). Reducing calcineurin inhibitor first for treating BK polyomavirus replication after kidney transplantation:long-term outcomes. Nephrol Dial Transplant;34(7):1240-50. doi: 10.1093/ndt/gfy346

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

Hocker B, et al (2019). Epidemiology and risk factors for BK polyomavirus replication and nephropathy in pediatric renal transplant recipients: an international CERTAIN Registry Study. Transplantation;103(6):1224-1233. doi: 10.1097/TP.0000000000002414

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

Keller N et al. (2019). Clinical utility of leflunomide for BK polyomavirus associated nephropathy in kidney transplant recipients: A multicenter retrospective study. Transpl Infect Dis;21(2):e13058. doi: 10.1111/tid.13058

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

Bicalho C, et al. (2018). Determination of viremia cut-off for risk to develop BKPyV-associated nephropathy among kidney transplant recipients. Transpl Infect Dis;20(5):e12969. doi: 10.1111/tid.12969

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

Nickeleit V, et al. (2018). The Banff Working Group classification of definitive polyomavirus nephropathy: morphologic definitions and clinical correlations. J Am Soc Nephrol;29(2):680-693.

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

Verghese P, et al (2017). The impact of recipient BKV shedding before transplant on BKV viruria, DNAemia, and nephropathy post-transplant: A prospective study. Pediatr Transplant;21(5). doi: 10.1111/petr.12942

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

Simard-Meilleur M, et al (2017). Stabilization of renal function after the first year of follow up in kidney transplant recipients for significant BK polyomavirus infection or BK polyomavirus-associated nephropathy. Transpl Infect Dis;19(3). doi: 10.1111/tid.12681.

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

Mallat et al. (2017) CMV and BKPyV infections in renal transplant recipients receiving an mTOR inhibitor-based regimen versus a CNI-based regimen: a systematic review and meta-analysis of randomized, controlled trials. Clin J Am Soc Nephrol; 12(8):1321-1336.

- 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

Arroyo D et al, (2014). Adjuvant ciprofloxacin for persistent BK polyomavirus infection in kidney transplant recipients. Journal of transplantation, 2014. Retrieved from https://www.hindawi.com/journals/jtrans/2014/107459/

- 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.

Humar A et al, (2014). Levofloxacin for BK Virus Prophylaxis Following Kidney Transplantation. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25399012

- 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

Jung, YH et al, (2013). Leflunomide therapy for BK virus allograft nephropathy after pediatric kidney transplantation. Pediatric transplantation, 17(2), E50-E54. Retrieved from www.ncbi.nlm.nih.gov/pubmed/23210794

- 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

Cibrik D et al, (2013). Randomized trial of everolimus-facilitated calcineurin inhibitor minimization over 24 months in renal transplantation. Transplantation. 95(7), 933-42. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23422495

- 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.

Dharnidharka VR et al, (2010). Retransplantation after BK nephropathy in prior kidney transplant: an OPTN database analysis. American Journal of Transplantation.10 (5), 1312-5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20353461

- 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.

Gabardi S et al, (2010). Evaluation of fluoroquinolones for the prevention of BK viremia after renal transplantation. Clinical Journal of the American Society of Nephrology. 5(7), 1298-304. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20507960

- 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.

Johnston O et al, (2010). Treatment of polyomavirus infection in kidney transplant recipients: a systemic review. Transplantation. 37(8), 3546-8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20090569

- 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.

Kuypers DRJ et al, (2009). A single-centre study of adjuvant cidofovir therapy for BK virus interstitial nephritis (BKVIN) in renal allograft recipients. Journal of Antimicrobial Chemotherapy. 63(2), 417-9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19056749

- 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.

Schold JD et al, (2009). Treatment for BK virus: incidence, risk factors and outcomes for kidney transplant recipients in the United States. Transplant International. 22(6), 626-34. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19207187

- 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.

Josephson MA et al, (2006). Treatment of renal allograft polyoma BK virus infection with leflunomide. Transplantation. 81(5), 704-10. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16534472

- 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.

Sener A et al, (2006). Intravenous immunoglobulin as a treatment for BK virus associated nephropathy: one-year follow-up of renal allograft recipients. Transplantation.81 (1), 117-20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16421486

- 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.

Brennan DC et al, (2005). Incidence of BK with tacrolimus versus cyclosporine and impact of preemptive immunosuppression reduction. American Journal of Transplantation. 5(3), 582-94. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15707414

- 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%.

Kuypers DRJ et al, (2005). Adjuvant low-dose cidofovir therapy for BK polyomavirus interstitial nephritis in renal transplant recipients. American Journal of Transplantation. 5(8), 1997-2004. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15996251

- 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).

Nickeleit V et al, (2000). Testing for polyomavirus type BK DNA in plasma to identify renal-allograft recipients with viral nephropathy. New England Journal of Medicine. 342(18), 1309-15. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10793163

- 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

Eid A et al (2019). Human Parvovirus B19 in solid organ transplantation: Guidelines from the American society of transplantaton infectious diseases community of practice. Clin Transplant;33:e13535. https://doi.org/10.1111/ctr.13535

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

Baek C et al (2017). Risk factors and long-term outcomes of parvovirus B19 infection in kidney transplant patients. Transpl Infect Dis;19(5). doi: 10.1111/tid.12754

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

Razonable RR et al, (2016). Not the Usual Viral Suspects: Parvovirus B19, West Nile Virus, and Human T-Cell Lymphotrophic Virus Infections After Kidney Transplantation. Seminars in nephrology. 36(5):428-434 retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27772627

- 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

Eid AJ et al, (2006). Parvovirus B19 infection after transplantation: a review of 98 cases. Clinical infectious diseases. 1;43(1):40-8. https://www.ncbi.nlm.nih.gov/pubmed/16758416

- 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

Qin J et al (2020). Perioperative Presentation of COVID-19 Disease in a Liver Transplant Recipient. Hepatology. 2020 March 27. https://www.ncbi.nlm.nih.gov/pubmed/32220017

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

Kumar D et al (2020). COVID-19: A Global Transplant Perspective on Successfully Navagating a Pandemic. Am J Transplant. 2020 March 23. https://www.ncbi.nlm.nih.gov/pubmed/32202064

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

Guillen E et al (2020). Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation? Am J Transplant. 2020 March 20. https://www.ncbi.nlm.nih.gov/pubmed/32198834

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

Manuek O et al (2019). RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;33:e13511. https://doi.org/10.1111/ctr.13511

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

Trang T et al (2018). Comparative effectiveness of aerosolized versus oral ribavirin for the treatment of respiratory syncytial virus infections: a single center retrospective cohort study and review of the literature. Transpl Infect Dis;20(2):e12844. doi: 10.1111/tid.12844

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

Natori Y et al (2018). A double-blind randomized trial of high-dose vs standard-dose influenza vaccine in adult solid organ transplant recipients. Clin Infect Dis;66(11):1698-1704. doi: 10.1093/cid/cix1082.

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

Burrows et al (2015). Oral ribavirin for respiratory syncytial virus infection after lung transplantation: Efficacy and cost-efficiency. J Heart Lung Transplant;34(7):958-62. doi: 10.1016/j.healun.2015.01.009

- 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

Ison M et al (2014). Outcome of influenza infection managed with oseltamivir in lung transplant recipients. J Heart Lung Transplant;27(3):282-288. doi: 10.1016/j.healun.2007.11.575.

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

Li L et al (2012). Oral versus inhaled ribavirin therapy for respiratory syncytial virus lower respiratory tract infection. J Heart Lung Transplant;28(1):67-71. doi: 10.1016/j.healun.2012.04.002

- Retrospective study investigating outcomes of oral versus inhaled ribavirin therapy

Kumar et al (2011). Influenza vaccination in the organ transplant recipient: review and summary recommendations. Am J Transplant;11(10):2020-2030. doi: 10.1111/j.1600-6143.2011.03753.x.

- Review article describing influenza vaccines in transplant recipients

Vu D et al. (2011) Respiratory viruses in lung transplant recipients: a critical review and pooled analysis of clinical studies. Am J Transplant;11(5):1071-1078.

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

Kumar et al (2010). Outcomes from pandemic influenza A H1N1 infection in recipients of solid organ transplants: a multicentre cohort study. Lancet Infect Dis;10(8):521-526. doi: 10.1016/S1473-3099(10)70133-X.

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

Palaez A et al (2009). Efficacy of oral ribavirin in lung transplant patients with respiratory syncytial virus lower respiratory tract infection. J Heart Lung Transplant;28(1):67-71. doi: 10.1016/j.healun.2008.10.008.

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

Hopkins, P.et al, (2008). Human metapneumovirus in lung transplant recipients and comparison to respiratory syncytial virus. American journal of respiratory and critical care medicine, 178(8), 876-881.Retrieved from www.ncbi.nlm.nih.gov/pubmed/18658110

- 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

Boeckh M et al, (2007). Randomized controlled multi-center trial of aerosolized ribavirin for respiratory syncytial virus upper respiratory tract infections in hematopoietic cell transplant recipients. Clin Infect Dis 44: 245–249. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/17173225

- 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

Glanville AR et al, (2005). Intravenous ribavirin is a safe and cost-effective treatment for respiratory syncytial virus infection after lung transplantation. J Heart Lung Transplant 24: 2114–2119. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16364859

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

Vilchez R et al (2003). Parainfluenza virus infection in adult lung transplant recipients: an emergent clinical syndrome with implications on allograft function. Am J Transplant;3(2):116-120. DOI: 10.1034/j.1600-6143.2003.00024.x

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

7.1.11 Measles

Liu, Y et al, (2015). Measles Virus Infection in Pediatric Liver Transplantation Recipients. Transplantation proceedings (Vol. 47, No. 9, pp. 2715-2718). Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26680079

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

Centers for Disease Control and Prevention (CDC). (2007) Multistate measles outbreak associated with an international youth sporting event--Pennsylvania, Michigan, and Texas, August-September, Morbidity and Mortality Weekly Report, 57, 169-173. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18288074

- 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.

Danerseau AM et al, (2008). Efficacy and safety of measles, mumps, rubella and varicella live viral vaccines in transplant recipients receiving immunosuppressive drugs. World journal of pediatrics. 4(4):254-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19104888

- 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

Warmington L, Lee BE, Robinson JL, (2005). Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatric Transplantation, 9, 311-314. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15910386

- 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

Arechabala MC, Catoni MI, Claro JC, Rojas NP, Rubio ME, Calvo MA, et al (2018). Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis. Cochrane Database Syst Rev.4:CD010597. https://www.ncbi.nlm.nih.gov/pubmed/29611180

- 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 tunneled CVC. The level of confidence of the conclusions is low.

Hentrich, M et al. (2014). Central venous catheter-related infections in hematology and oncology: 2012 updated guidelines on diagnosis, management and prevention by the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology. Annals of Oncology, 00, 1-12. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24399078

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

O'Grady, N et al. (2011) Guidelines for the prevention of intravascular catheter-related infections. Clinical Infectious Diseases, 52(9), e162-e193. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21460264

- IDSA guidelines for prevention of catheter- related infections.

Bouza, E, Burillo, A, Buembe, M. (2011). Managing intravascular catheter-related infections in heart transplant patients: how far can we apply IDSA guidelines for immunocompromised patients? Current Opinion in Infectious Disease, 24(4), 302-308. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21666455

- 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.

Soothill, J et al. (2009). A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hemopoietic stem cell transplant ward. American Journal of Infection Control, 37(8), 626-630. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19616869

- 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.

Vokurka S, Kabatova-Maxova K, Skardova J, Bystricka E. (2009). Antimicrobial chlorhexidine/ silver sulfadiazine-coated central venous catheters versus those uncoated in patients undergoing allogeneic stem cell transplantation. Support Care Cancer, 17, 145–151. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18449570

- 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

Subramanian AK, Theodoropoulos NM; Infectious Diseases Community of Practice of the American Society of Transplantation. Mycobacterium tuberculosis infections in solid organ transplantation: Guidelines from the infectious diseases community of practice of the American Society of Transplantation (2019). Clin Transplant. 33(9):e13513. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30817030

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

Abad CL, Deziel PJ, Razonable RR (2019). Treatment of latent TB infection and the risk of tuberculosis after solid organ transplantation: comprehensive review. Transplant Infect Dis.21:e13178. Retrieved from https://onlinelibrary.wiley.com/doi/full/10.1111/tid.13178

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

Simkins J, Abbo LM, et al (2017). Twelve-Week Rifapentine Plus Isoniazid Versus 9-Month Isoniazid for the Treatment of Latent Tuberculosis in Renal Transplant Candidates. Transplantation.101(6):1468-1472. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27548035

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

Nahid P, Dorman SE, Alipanah N, et al (2016). Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis.63.147-95. Retrieved from https://academic.oup.com/cid/article/63/7/e147/2196792

- IDSA guidelines for drug susceptible TB

Sun HY, Munoz P, Torre-cisneros J, et al (2013). Mycobacterium tuberculosis-associated immune reconstitution syndrome in solid-organ transplant recipients. Transplantation. 95:1173-81. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/23435454

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

Morris MI, Daly JS, Blumberg E, et al (2012). Diagnosis and management of tuberculosis in transplant donors: a donor-derived infections consensus conference report. Am J Transplant.12:2288-300. Retrieved from http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2012.04205.x/full

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

Currie AC, Knight SR, Morris PJ (2010).Tuberculosis in renal transplant recipients: the evidence for prophylaxis. Transplantation.90(7):695-704. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/20647975

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

Aguado JM, Torre-cisneros J, Fortún J, et al (2009). Tuberculosis in solid-organ transplant recipients: consensus statement of the group for the study of infection in transplant recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology. Clin Infect Dis.48:1276-84. Retrieved from https://academic.oup.com/cid/article/48/9/1276/409456

- 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.

Torre-cisneros J, Doblas A, Aguado JM, et al (2009). Tuberculosis after solid-organ transplant: incidence, risk factors, and clinical characteristics in the RESITRA (Spanish Network of Infection in Transplantation) cohort. Clin Infect Dis.48(12):1657-65. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed?term=19445585

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

7.2.3 Nontuberculosis Mycobacterium

Longworth SA, Daly JS (2019); AST Infectious Diseases Community of Practice. Management of infections due to nontuberculous mycobacteria in solid organ transplant recipients-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13588. Retrieved from https://onlinelibrary.wiley.com/doi/full/10.1111/ctr.13588

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

Friedman DZP, Cervera C, Halloran K, Tyrrell G, Doucette K (2019). Non-tuberculous mycobacteria in lung transplant recipients: prevalence, risk factors, and impact on survival and chronic lung allograft dysfunction. Transpl Infect Dis.00:e13229. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31794120

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

Griffith DE, Eagle G, et al (2018). Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by Mycobacterium avium Complex (CONVERT). A Prospective, Open-Label, Randomized Study. Am J Respir Crit Care Med.15;198(12):1559-1569. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30216086

- Data to support use of inhaled amikacin in refractory cases

Griffith DE, Aksamit T, Brown-Elliot BA, et al. (2018). An official ATS/IDSA Statement: Diagnosis, treatment and prevention of nontuberculosis mycobacterial diseases. Am J Respir Crit Care Med.175, 367-416. Retrieved from http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/NTM%20Disease.pdf

- IDSA guideline, update in progress as of 2018.

Doucette K, Fishman JA. (2004). Nontuberculous mycobacterial infection in hematopoietic stem cell and solid organ transplant recipients. Clinical Infectious Diseases. 38(10):1428-1439. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/15156482

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

Johnson MM, Odell JA (2004). Nontuberculous mycobacterial pulmonary infections. J Throac Dis.6(3):210-220. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/24624285

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

Vanermarliere A, Van Audenhove A, Peetermans WE, et al (2003). Mycobacterial infection in renal transplantation in Western population. Transplant Infectious Disease. 5(1):9-15. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12791069.

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

Queipo JA, Broseta B, Santos M, et al (2003). Mycobacterial infection in a series of 1261 renal transplant recipients. Clinical microbiology and infection. 9(6):518-525.Retrieved from http://onlinelibrary.wiley.com/doi/10.1046/j.1469-0691.2003.00532.x/full.

- 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

Restrepo A, Clark NM (2019); Infectious Diseases Community of Practice of the American Society of Transplantation. Nocardia infections in solid organ transplantation: Guidelines from the Infectious Diseases Community of Practice of the American Society of Transplantation. Clin Transplant. 33(9):e13509. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30817024

- AST IDCOP 2019 update for Nocardia

Hemmersbach-Miller M, Stout JE, et al (2018). Nocardia infections in the transplanted host.Transpl Infect Dis.20(4):e12902. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/29668123

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

Coussement J, Lebeaux D, et al (2016). Nocardia Infection in Solid Organ Transplant Recipients: A Multicenter European Case-control Study. Clin Infect Dis.63(3):338-45. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27090987

- 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.

Woods GL, Brown-Elliott BA, Conville PS, Desmond EP, Hall GS, Lin G, Pfyffer GE, Ridderhof JC, Siddiqi SH, Wallace RJ Jr, Warren NG, Witebsky FG.2011 Mar.

- CLSI reporting standards for susceptibility of nocardia

Uhde KB, et al, (2010). Antimicrobial-resistant Nocardia isolates, United States, 1995–2004. Clin Infect Dis, 51(12):1445-1448. Retrieved from https://academic.oup.com/cid/article/51/12/1445/317352.

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

Peleg AY, Husain S, et al (2007). Risk factors, clinical characteristics, and outcome of Nocardia infection in organ transplant recipients: a matched case-control study. Clin Infect Dis. 15;44(10):1307-14. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/17443467

- 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

Park SY, Jung JH, Kwon H et al (2020). Epidemiology and risk factors associated with Pneumocystis jirovecii pneumonia in kidney transplant recipients after 6-month trimethoprim-sulfamethoxazole prophylaxis: a case-control study. Transpl Infect Dis. E13245. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31943590

- 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.

Fishman JA, Gans H (2019); AST Infectious Diseases Community of Practice. Pneumocystis jiroveci in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant.33(9):e13587. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31077616

- AST IDCOP 2019 Updates to Management of PCP

Hosseini-Moghaddam SM, Shokoohi M, et al (2019). A Multicenter Case-control Study of the Effect of Acute Rejection and Cytomegalovirus Infection on Pneumocystis Pneumonia in Solid Organ Transplant Recipients. Clin Infect Dis.68(8):1320-1326. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30107568

- 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.

Gabardi S et al. (2012). Atovaquone versus trimethoprim-sulfamethoxazole as Pneumocystis jirovecii pneumonia prophylaxis following renal transplantation. Clinical Transplantation, 26(3), E184-90.Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/22487221

- 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.

Wang EH, et al. (2012). Pneumocystis pneumonia in solid organ transplant recipients: not yet an infection of the past. Transplant Infectious Disease, 14(5):519-25. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22571389

- 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.

Anand S, et al. (2011). Pneumocystis jirovecii pneumonia is rare in renal transplant recipients receiving only one month of prophylaxis. Transplant Infectious Disease, 13(6):570-4. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22093215

- 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.

El-Sadr WM et al. (1998). Atovaquone compared with dapsone for the prevention of Pneumocystis carinii pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. Community Program for Clinical Research on AIDS and the AIDS Clinical Trials Group. New England Journal of Medicine, 339(26):1889-95. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9862944

- 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.

Ioannidis JP et al. (1996). A meta-analysis of the relative efficacy and toxicity of Pneumocystis carinii prophylactic regimens. Archives of Internal Medicine, 156(2), 177-88. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8546551

- 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.

Barber BA et al. (1996). Clindamycin/primaquine as prophylaxis for Pneumocystis carinii pneumonia. Clinical Infectious Disease, 23(4),718-22. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8909833

- 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.

Warnock AC, Rimland D (1996). Comparison of trimethoprim-sulfamethoxazole, dapsone, and pentamidine in the prophylaxis of Pneumocystis carinii pneumonia. Pharmacotherapy.16(6):1030-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/8947975.

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

Sistek CJ, Wordell CJ, Hauptman SP (1992). Adjuvant corticosteroid therapy for Pneumocystis carinii pneumonia in AIDS patients. Ann Pharmacother.26(9):1127-33. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/1421680

- 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

Husain S, Camargo JF (2019). Invasive Aspergillosis in solid-organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13544. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30900296

- AST IDCOP 2019 updates for aspergillosis

Ullmann AJ, Aguado JM, et al (2018). Diagnosis and management of Aspergillus diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline. Clin Microbiol Infect. 2018 May;24 Suppl 1:e1-e38. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/29544767

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

Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;63:e1-e60. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27365388

- IDSA guidelines for aspergillosis

Maertens JA, Raad II, Marr KA, et al (2016). Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a phase 3,

randomised-controlled, non-inferiority trial. Lancet.387:760-9. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26684607

- 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.

Marr KA, Schlamm HT, Herbrecht R, et al (2015). Combination antifungal therapy for invasive aspergillosis: a randomized trial. Ann Intern Med.162:81-9. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25599346

- 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.

Pascual A, Csajka C, Buclin T, Bolay S, Bille J, Calandra T, Marchetti O (2012). Challenging recommended oral and intravenous voriconazole doses for improved efficacy and safety: population pharmacokinetics-based analysis of adult patients with invasive fungal infections. Clin Infect Dis.55(3):381-90. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/22610925

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

Pfeiffer CD, Fine JP, Safdar N (2006). Diagnosis of invasive aspergillosis using a galactomannan assay: a meta-analysis. Clin Infect Dis. 42:1417-27. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16619154

- 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.

Gavalda J, Len O, San juan R, et al (2005). Risk factors for invasive aspergillosis in solid-organ transplant recipients: a case-control study. Clin Infect Dis.41:52-9. Retrieved from https://academic.oup.com/cid/article/41/1/52/325103

- 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.

Drew RH, Dodds Ashley E, Benjamin DK, Duane davis R, Palmer SM, Perfect JR (2004). Comparative safety of amphotericin B lipid complex and amphotericin B deoxycholate as aerosolized antifungal prophylaxis in lung-transplant recipients. Transplantation.77:232-7. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/14742987.

- 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.

Helmi M, Love RB, Welter D, Cornwell RD, Meyer KC (2003). Aspergillus infection in lung transplant recipients with cystic fibrosis: risk factors and outcomes comparison to other types of transplant recipients. Chest.123:800-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12628881.

- 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.

Herbrecht R, Denning DW, et al (2002). Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med.347(6):408-15. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12167683

- 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

Baddley JW, Forrest GN (2019); AST Infectious Diseases Community of Practice. Cryptococcosis in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13543. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30900315

- AST IDCOP 2019 updates for cryptococcosis

Marinelli T, Anagnostou N, Daniel S, Wigg AJ, Teh J (2019). Very early onset of Cryptococcus neoformans disease following liver transplantation: report of two cases and a review of the literature. Transpl Infect Dis.22;e13227. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31785187

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

Perfect JR, et al, (2010). Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis, 50(3):291-322. Retrieved from https://academic.oup.com/cid/article/50/3/291/392360

- 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.

Sun H, et al, (2009). Lipid Formulations of Amphotericin B Significantly Improve Outcome in Solid Organ Transplant Recipients with Central Nervous System Cryptococcosis. Clin Infect Dis, 49(11):1721-1728. Retrieved from https://doi.org/10.1086/647948.

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

Dromer F, et al, (2008). Major role for amphotericin B–flucytosine combination in severe cryptococcosis. PLoS ONE. 3(8):e2870. Retrieved from http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0002870.

- 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

Leitheiser S, Harner A, Waller J, et al (2020). Risk factors associated with invasive fungal infections in kidney transplant patients. Am J Med Sci. 3599(2):108-116. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31836132.

- 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.

Kullberg BJ, Viscoli C, et al (2019). Isavuconazole Versus Caspofungin in the Treatment of Candidemia and Other Invasive Candida Infections: The ACTIVE Trial. Clin Infect Dis. 68(12):1981-1989. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30289478

- Non-inferiority of isavuconazole to caspofungin was not shown

Aslam S, Rotstein C; AST Infectious Disease Community of Practice. Candida infections in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13623. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31155770

- AST IDCOP 2019 updates to management of candida in SOT

Bidaud AL, Chowdhary A, Dannaoui E (2018). Candida auris: An emerging drug resistant yeast - A mini-review. J Mycol Med. 28(3):568-573. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30030072

- Updated review on Candida auris

Pappas PG,Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE, Sobel JD. Clinical practice guideline for the management of candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016;62(4):e1–50
https://academic.oup.com/cid/article/62/4/e1/2462830

- IDSA 2016 guidelines for treatment of candidiasis.

Eschenauer GA, Kwak EJ, Humar A, Potoski BA, Clarke LG, Shields RK, et al (2015). Targeted versus universal antifungal prophylaxis among liver transplant recipients. Am J Transplant.15(1):180-189. https://onlinelibrary.wiley.com/doi/10.1111/ajt.12993

- 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.

Gavalda J, Meije Y, Fortun J, Roilides E, Lortholary O, Munoz P, et al (2014). Invasive fungal infections in solid organ transplant recipients. Clin Microbiol Infect 20(7):27–48.
https://www.sciencedirect.com/science/article/pii/S1198743X14605000?via%3Dihub

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

Singh N, Huprikar S, Burdette SD, Morris MI, Blair JE, Wheat LJ, and the AST, Infectious Disease Community of Practice, Donor-Derived Fungal Infection Working Group. Am J Transplant. 2012;12:2414-2428. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-6143.2012.04100.x.

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

Reboli AC, Rotstein C, et al (2007). Anidulafungin versus fluconazole for invasive candidiasis. N Engl J Med. 356(24):2472-82. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/17568028

- Andidafungin was non-inferior to fluconazole with a favorable response in the andidafungin arm.

Mora-Duarte J, Betts R, et al (2002); Caspofungin Invasive Candidiasis Study Group. Comparison of caspofungin and amphotericin B for invasive candidiasis. N Engl J Med. 347(25):2020-9. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12490683

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

7.3.5 Histoplasmosis

Miller R, Assi M (2019); AST Infectious Diseases Community of Practice. Endemic fungal infections in solid organ transplant recipients-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13553. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30924967

- AST IDCOP 2019 updates on managements of endemic fungal infections

Thompson GR III, Rendon A, Ribeiro dos Santos R, Queiroz-Telles F, Ostrosky-Zeichner L, Azie N, et al (2016). Isavuconazole treatment of Cryptococcosis and dimorphic mycoses. Clin Infect Dis.63(3):356-362. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946023/

- "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.

Kauffman CA and Miceli M (2015). Histoplasmosis and Blastomycosis in Solid Organ Transplant Recipients. J Fungi. 1(2):84-106. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5753102/

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

Kauffman CA, Freifeld AG, Andes DR, Baddley JW, Herwaldt L, Walker RC, et al (2014). Endemic fungal infections in solid organ and hematopoeitic cell transplant recipients enrolled in TRANSNET. Transpl Infect Dis.16(2):213-224. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5664161/

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

Assi M, Martin S, Hage C, Frefield A, Avery R, Baddley JW, et al (2013). Histoplasmosis after solid organ transplant. Clin Infect Disease.57(11):1542-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3814825/

- 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.

Wheat JL, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, Kauffman CA. Clinical practice guidelines for the management of patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2007; 45:807–25. https://academic.oup.com/cid/article/45/7/807/541502

- IDSA 2007 guidelines for treatment of histoplasmosis.

7.4 Other

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

Wolfe CR, Ison MG (2019); AST Infectious Diseases Community of Practice. Donor-derived infections: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13547. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30903670

- AST IDCOP 2019 Guidelines on donor-derived infections

Fishman JA (2017). Infection in Organ Transplantation. American Journal of Transplantation.17:856-879. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/28117944

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

Green, M. (2013). Introduction: Infections in Solid Organ Transplantation. American Journal of Transplantation, 13: 3–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23464993

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

Fishman, JA et al. (2010). Infection in Organ Transplantation: Risk Factors and Evolving Patterns of Infection. Infect Dis Clin N Am, 24, 273–283. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20466270

- This article reviews risk factors for and patterns of infections post-transplant.

Sun HY, et al, (2010). Unrecognized pretransplant and donor-derived cryptococcal disease in organ transplant recipients. Clinical Infectious Diseases, 51(9):1062-1069. Retrieved from https://academic.oup.com/cid/article/51/9/1062/292746.

- Retrospective review of solid organ transplant recipients who developed cryptococcosis post-transplant, including nine who developed infection within 30 days which could indicate unrecognized pretransplant or donor-derived cryptococcosis.

Fishman, JA et al. (2009). Introduction: Infection in Solid Organ Transplant Recipients. American Journal of Transplantation, 9 (Suppl 4): S3–S6. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20070692

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

Fishman, JA. (2007). Infection in Solid-Organ Transplant Recipients. N Engl J Med, 357, 2601-14. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18094380

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

Humar, A. et al. (2006). American Society of Transplantation Recommendations for Screening, Monitoring and Reporting of Infectious Complications in Immunosuppression Trials in Recipients of Organ Transplantation. American Journal of Transplantation, 6: 262–274. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16426310

- 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.

Snydman, DR et al. (2001). Epidemiology of Infections after Solid-Organ Transplantation. Clinical Infectious Diseases, 33 (Suppl 1), S5–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11389515

- 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.

Freeman RB, et al, (1999). Outcome of transplantation of organs procured from bacteremic donors. Transplantation, 68(8):1107-1111. Retrieved from https://journals.lww.com/transplantjournal/Abstract/1999/10270/OUTCOME_OF_TRANSPLANTATION_OF_ORGANS_PROCURED_FROM.8.aspx.

- 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

Centers for Disease Control and Prevention (CDC). (2007) Multistate measles outbreak associated with an international youth sporting event--Pennsylvania, Michigan, and Texas, August-September, Morbidity and Mortality Weekly Report, 57, 169-173. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18288074

- 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.

Warmington L, Lee BE, Robinson JL. (2005). Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatric Transplantation, 9, 311-314. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15910386

- 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

Pergam SA, Limaye AP (2013). Varicella zoster virus in solid organ transplantation. Am J Transplant.13 Suppl 4:138-46. Retreived from https://www.ncbi.nlm.nih.gov/pubmed/20070670

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

Arora A, Mendoza N, Brantley J, Yates B, Dix L, Tyring S. (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. Journal of Infectious Diseases, 197, 1289-1295.Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18422441

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

Tyring S, Belanger R, Bezwoda W, Ljungman P, Boon R, Saltzman RL; Collaborative Famciclovir Immunocompromised Study Group. (2001). A randomized, double-blind trial of famciclovir versus acyclovir for the treatment of localized dermatomal herpes zoster in immunocompromised patients. Cancer Investigation, 19, 13-22. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11291551

- 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

Shepp DH, Dandliker PS, Meyers JD. (1986). Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. New England Journal of Medicine, 314, 208-212. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/3001523

- 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

Yue MC, Collins JT, Subramoniapillai E, Kennedy GA (2017). Successful use of oseltamivir prophylaxis in managing a nosocomial outbreak of influenza A in a hematology and allogeneic stem cell transplant unit. Asia Pac J Clin Oncol.13(1):37-43. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27730741

- 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 MMWR: Guidelines for the investigation of contacts of persons with infectious tuberculosis. 2005;54(RR15):1-37. Retrieved from https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

- CDC guidelines for evaluating patients at risk for developing TB after an exposure. Includes as 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

CDC Guidance for the evaluation and public health management of suspected outbreaks of meningococcal disease. Retrieved from https://www.cdc.gov/meningococcal/downloads/meningococcal-outbreak-guidance.pdf

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

7.4.3 Immunizations

Danziger-Isakov L, Kumar D; AST ID Community of Practice. Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice. Clin Transplant. 2019 Sep;33(9):e13563. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31002409

- AST IDCOP 2019 updates on vaccinations

Buchan CA, Kotton CN; AST Infectious Diseases Community of Practice. Travel medicine, transplant tourism, and the solid organ transplant recipient-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13529. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30859623

- 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

Vink P, Ramon Torrell JM, et al (2019). Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: a Phase III, Randomized Clinical Trial. Clin Infect Dis. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30843046

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

Natori Y, Shiotsuka M, et al (2018). A Double-Blind, Randomized Trial of High-Dose vs Standard-Dose Influenza Vaccine in Adult Solid-Organ Transplant Recipients. Clin Infect Dis. 66(11):1698-1704. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/29253089

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

Cordero E, Roca-Oporto C, et al (2017). Two Doses of Inactivated Influenza Vaccine Improve Immune Response in Solid Organ Transplant Recipients: Results of TRANSGRIPE 1-2, a Randomized Controlled Clinical Trial. Clin Infect Dis.64(7):829-838. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/28362949

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

Rubin LG, Levin MJ, Ljungman P et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2013; epub ahead of print 4 Dec 2013. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24311479

- 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

Ramanan P, Scherger S, Benamu E et al (2020). Toxoplasmosis in non-cardiac solid organ transplant recipients: a case series and review of literature. Transpl Infect Dis. 22e13218. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/31769583

- 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.

Hoz R et al (2019). Tissue and blood protozoa including toxoplasmosis, Chagas disease, leishmaniasis, Babesia, Acanthamoeba, Balamuthia, and Naegleria in solid organ transplant recipients – Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;33:e13546 Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30900295

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

Cherhrazi-Raffle A, et al (2015). Toxoplasma gondii serology and outcomes after heart transplantation: contention in the literature. Transplant Proceedings.47(6):1949-1953. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26293079

- 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.

Fernandez-Sabe N et al (2012). Risk factors, clinical features and outcomes of toxoplasmosis in solid-organ transplant recipients: a matched case-control study. Clin Inf Dis. 54(3):355-361.

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

Derouin F, Pelloux H (2008). Prevention of toxoplasmosis in transplant patients. Clin Microbio Infect. 2008; 14:1089-1101. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19018809.

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

Wreghitt TG, et al. (1995). Antibiotic prophylaxis for the prevention of donor-acquired toxoplasmoa gondii infection in transplant patients. Journal of Infection. 31(3):253-254. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/8586854

- Summary of literature discussing chemoprophylaxis of toxoplasmosis infection.