

**Title:** Up in the Air: Optimizing Induction Immunosuppression in Lung Transplantation

**Presenter:**

Leah Georgiades, PharmD

PGY1 Pharmacy Resident

UPMC Presbyterian

**Date:** 2/5/2025

**Learning Objectives:**

1. Describe the immunology, prevalence, and risk factors of acute cellular rejection in lung transplant recipients.
2. Discuss current evidence and trends regarding induction immunosuppressive therapy following lung transplantation.
3. Identify opportunities for optimization of induction immunosuppression based on clinical evidence and patient-specific factors.

**Abstract:**

There is limited evidence regarding the efficacy of induction immunosuppression in lung transplantation. Furthermore, there is a lack of established guidance regarding selection of the optimal induction agent. This gap in knowledge exists in both the risks and benefits of varying agents, in addition to their significance in the context of patient-specific factors.

The primary goals of this presentation are to provide an overview of the pathophysiology and epidemiology of acute cellular rejection in lung transplant recipients, as well as prevention with induction immunosuppression therapy. Next, trends in clinical practice regarding induction immunosuppression in lung transplant and evidence regarding efficacy of treatment and comparison of strategies, including data from specific patient populations will be analyzed. Finally, a recommendation will be provided to optimize the current protocol utilized within our institution.

A comprehensive review of relevant studies and national registry data was utilized to inform the presentation.

Significant findings of the presentation indicate a preferred induction agent in patients with short telomeres and further guidance on stratifying patients with higher risk for infections when selecting an induction therapy strategy. Additionally, there is an opportunity identified for lowering therapeutic targets of maintenance

immunosuppression therapy with a particular induction agent, which may be relevant in minimizing certain adverse events.

The efficacy of induction immunosuppression in lung transplantation is established and clarity regarding the role of certain patient-specific factors in clinical decision making is applied to the current institutional protocol.

**Knowledge Check Questions:**

1. What is the primary function of the Human Leukocyte Antigen (HLA) system?
  - A. Antibody Production
  - B. Cytokine Production
  - C. Presentation of antigens to T-cells
  - D. B-cell Activation
  
2. What is the main role of induction immunosuppression immediately post-lung transplant?
  - A. Prevention of infection post-transplant
  - B. Treatment of acute rejection
  - C. Prevention of chronic rejection
  - D. Prevention of acute rejection
  
3. What induction immunosuppression strategy has demonstrated the greatest reduction in acute rejection outcomes in the first year post-lung transplant?
  - A. No induction
  - B. ATG
  - C. Alemtuzumab
  - D. Basiliximab

## References:

1. 2020 International Thoracic Organ Transplant (TTX) Registry Data
2. 2022 OPTN SRTR Annual Data Report
3. Kumbala D, Zhang R. Essential concept of transplant immunology for clinical practice. *World J Transplant*. 2013 Dec 24;3(4):113-8. doi: 10.5500/wjt.v3.i4.113.
4. Levine D, Hachem R. Lung Allograft Rejection. *Thoracic Surgery Clinics*. 2022 May 1; 32(2): 221-229.
5. Todd J et al. Risk Factors for Acute Rejection in the First Year after Lung Transplant. A Multicenter Study. *Am J Respir Crit Care Med*. 2020 May 7; 202(4). doi: 10.1164/rccm.201910-1915OC.
6. Renaud-Picard B, Koutsokera A, Cabanero M, Martinu T. Acute Rejection in the Modern Lung Transplant Era. *Semin Respir Crit Care Med*. 2021 Jun;42(3):411-427. doi: 10.1055/s-0041-1729542.
7. Fredrick SR, Iasella CJ, Sacha LM, Rivosecchi RM, Morrell MR, Sanchez PG, Pilewski JM, Snyder ME, McDyer JF, Moore CA. Incidence of Acute Cellular Rejection After Granulocyte Colony-Stimulating Factor in Lung Transplant Recipients. *J Pharm Pract*. 2024 Aug;37(4):830-837. doi: 10.1177/08971900231184308.
8. Greer M, Werlein C, Jonigk D. Surveillance for acute cellular rejection after lung transplantation. *Ann Transl Med*. 2020 Mar;8(6):410. doi: 10.21037/atm.2020.02.127.
9. McDermott JK, Girgis RE. Individualizing immunosuppression in lung transplantation. *Glob Cardiol Sci Pract*. 2018 Mar 14;2018(1):5. doi: 10.21542/gcsp.2018.5.
10. Chung PA, Dilling DF. Immunosuppressive strategies in lung transplantation. *Ann Transl Med*. 2020 Mar;8(6):409. doi: 10.21037/atm.2019.12.117.
11. Landino SM, Nawalaniec JT, Hays N, Osho AA, Keller BC, Allan JS, Keshavjee S, Madsen JC, Hachem R. The role of induction therapy in lung transplantation. *Am J Transplant*. 2024 Nov 16:S1600-6135(24)00695-6. doi: 10.1016/j.ajt.2024.11.011.
12. Palmer SM, Miralles AP, Lawrence CM, Gaynor JW, Davis RD, Tapson VF. Rabbit antithymocyte globulin decreases acute rejection after lung transplantation: results of a randomized, prospective study. *Chest*. 1999 Jul;116(1):127-33. doi: 10.1378/chest.116.1.127.
13. Whitson BA, Lehman A, Wehr A, Hayes D Jr, Kirkby S, Pope-Harman A, Kilic A, Higgins RS. To induce or not to induce: a 21st century evaluation of lung

- transplant immunosuppression's effect on survival. *Clin Transplant*. 2014 Apr;28(4):450-61. doi: 10.1111/ctr.12339.
14. Shagabayeva L, Osho AA, Moonsamy P, Mohan N, Li SS, Wolfe S, Langer NB, Funamoto M, Villavicencio MA. Induction therapy in lung transplantation: A contemporary analysis of trends and outcomes. *Clin Transplant*. 2022 Nov;36(11):e14782. doi: 10.1111/ctr.14782
  15. Furukawa M, Chan EG, Ryan JP, Hyzny EJ, Sacha LM, Coster JN, Pilewski JM, Lendermon EA, Kilaru SD, McDyer JF, Sanchez PG. Induction Strategies in Lung Transplantation: Alemtuzumab vs. Basiliximab a Single-Center Experience. *Front Immunol*. 2022 Jun 1;13:864545. doi: 10.3389/fimmu
  16. Furuya Y, Jayarajan SN, Taghavi S, Cordova FC, Patel N, Shiose A, Leotta E, Criner GJ, Guy TS, Wheatley GH, Kaiser LR, Toyoda Y. The Impact of Alemtuzumab and Basiliximab Induction on Patient Survival and Time to Bronchiolitis Obliterans Syndrome in Double Lung Transplantation Recipients. *Am J Transplant*. 2016 Aug;16(8):2334-41. doi: 10.1111/ajt.13739.
  17. Li KHC, Ho JCS, Recaldin B, Gong M, Ho J, Li G, Liu T, Wu WKK, Wong MCS, Xia Y, Dong M, Tse G; International Health Informatics Study Network. Acute Cellular Rejection and Infection Rates in Alemtuzumab vs Traditional Induction Therapy Agents for Lung and Heart Transplantation: A Systematic Review and Meta-analysis. *Transplant Proc*. 2018 Dec;50(10):3723-3731. doi: 10.1016/j.transproceed.2018.08.044.
  18. Courtwright AM, El-Chemaly S. Telomeres in Interstitial Lung Disease: The Short and the Long of It. *Ann Am Thorac Soc*. 2019 Feb;16(2):175-181. doi: 10.1513/AnnalsATS.201808-508CME.
  19. Courtwright AM, Lamattina AM, Takahashi M, Trindade AJ, Hunninghake GM, Rosas IO, Agarwal S, Raby BA, Goldberg HJ, El-Chemaly S. Shorter telomere length following lung transplantation is associated with clinically significant leukopenia and decreased chronic lung allograft dysfunction-free survival. *ERJ Open Res*. 2020 Jun 15;6(2):00003-2020. doi: 10.1183/23120541.00003-2020.
  20. Hannan SJ, Iasella CJ, Sutton RM, Popescu ID, Koshy R, Burke R, Chen X, Zhang Y, Pilewski JM, Hage CA, Sanchez PG, Im A, Farah R, Alder JK, McDyer JF. Lung transplant recipients with telomere-mediated pulmonary fibrosis have increased risk for hematologic complications. *Am J Transplant*. 2023 Oct;23(10):1590-1602. doi: 10.1016/j.ajt.2023.06.014.
  21. Vadnerkar A, Toyoda Y, Crespo M, Pilewski J, Mitsani D, Kwak EJ, Silveira FP, Bhamra J, Shields R, Bermudez C, Clancy CJ, Nguyen MH. Age-specific complications among lung transplant recipients 60 years and older. *J Heart Lung Transplant*. 2011 Mar;30(3):273-81. doi: 10.1016/j.healun.2010.08.032.
  22. Iasella CJ, Winters SA, Kois A, Cho J, Hannan SJ, Koshy R, Moore CA, Ensor CR, Lendermon EA, Morrell MR, Pilewski JM, Sanchez PG, Kass DJ, Alder JK,

Nouraie SM, McDyer JF. Idiopathic pulmonary fibrosis lung transplant recipients are at increased risk for EBV-associated posttransplant lymphoproliferative disorder and worse survival. *Am J Transplant*. 2020 May;20(5):1439-1446. doi: 10.1111/ajt.15756.

23. Jaksch P, Ankersmit J, Scheed A, Kocher A, Muraközy G, Klepetko W, Lang G. Alemtuzumab in lung transplantation: an open-label, randomized, prospective single center study. *Am J Transplant*. 2014 Aug;14(8):1839-45. doi: 10.1111/ajt.12824.
24. Whited LK, Latran MJ, Hashmi ZA, Wang IW, Wozniak TC, Duncan MD, Roe DW, Baz MA, Hage CA. Evaluation of Alemtuzumab Versus Basiliximab Induction: A Retrospective Cohort Study in Lung Transplant Recipients. *Transplantation*. 2015 Oct;99(10):2190-5. doi: 10.1097/TP.0000000000000687.