Clinical Trials in Solid Organ Transplant, What is on the Horizon?

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Disclosures

No relevant financial disclosures

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Objectives

Review	Review the current state of research in solid organ transplantation
Discuss	Discuss upcoming clinical trials and opportunities in solid organ transplantation research
Examine	Examine the ongoing need for research in solid organ transplantation

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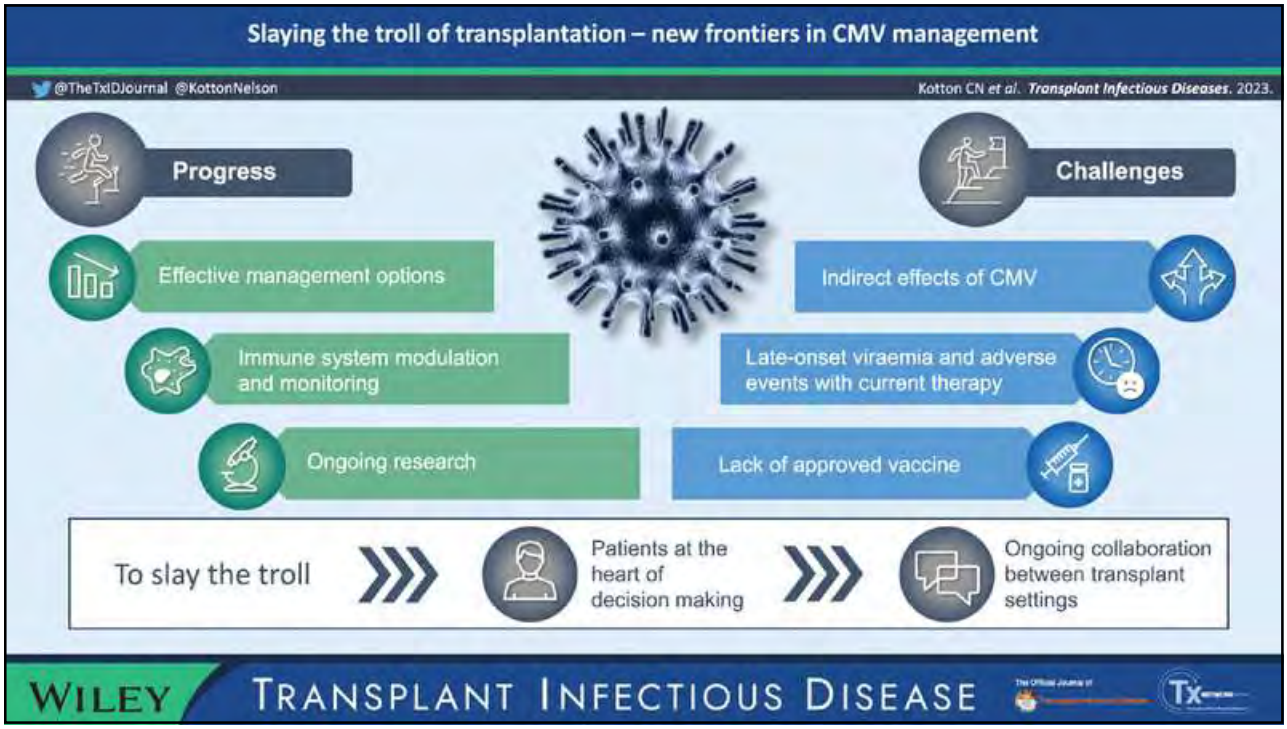

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CMV Prevention

- Preemptive therapy
- Immunomodulation
- Vaccination

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JAMA Network

From: **Effect of Preemptive Therapy vs Antiviral Prophylaxis on Cytomegalovirus Disease in Seronegative Liver Transplant Recipients With Seropositive Donors: A Randomized Clinical Trial**

JAMA. 2020;323(14):1378-1387. doi:10.1001/jama.2020.3138

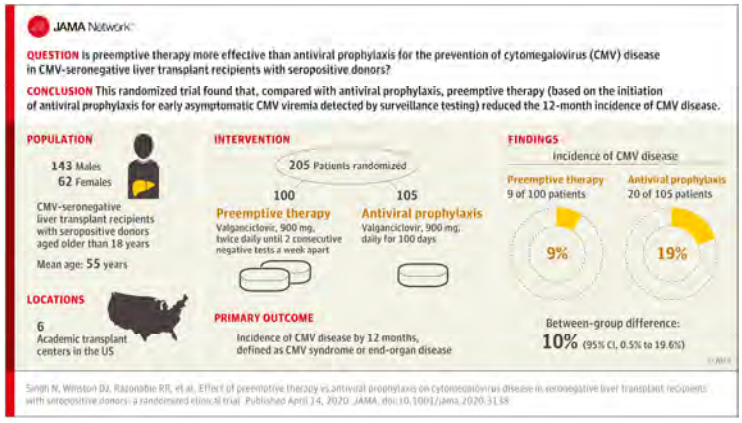

Figure Legend:
Effect of Preemptive Therapy vs Antiviral Prophylaxis on CMV Disease in Seronegative Liver Transplant Recipients With Seropositive Donors

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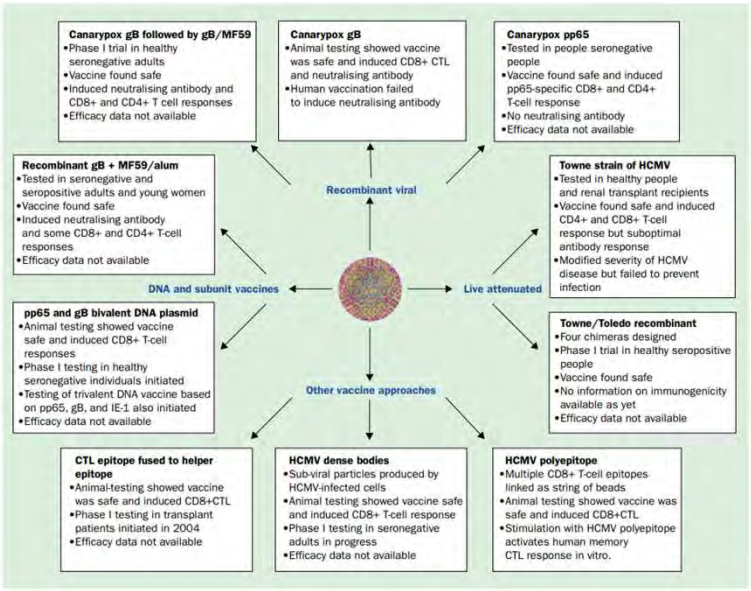
CMV vaccines, where are we now?



Maher K Gandhi and Rajiv Khanna. *The Lancet Infectious Diseases.* 2004 Dec; 4(12):725-738

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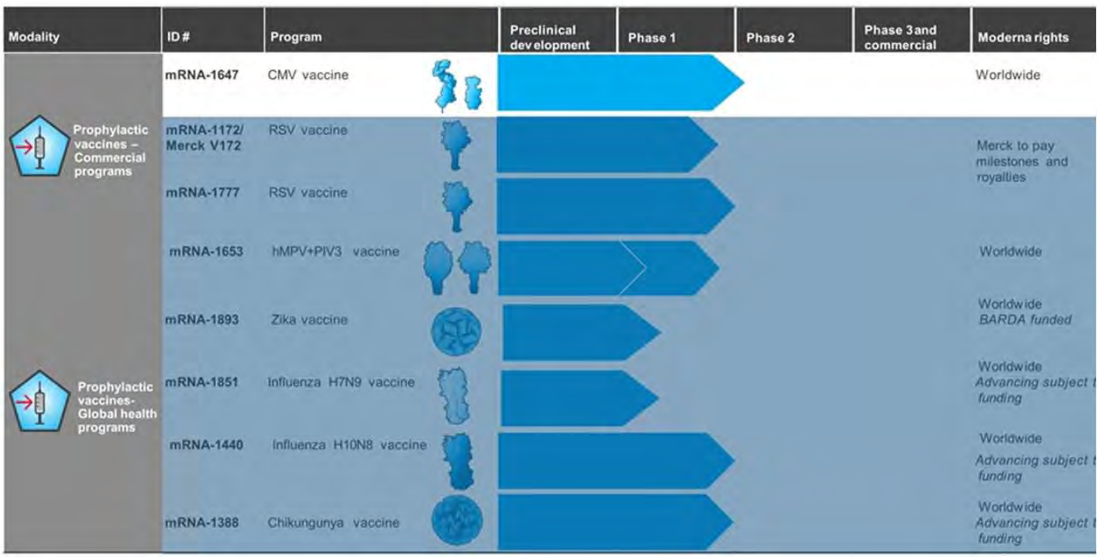

https://trials.modernatx.com/study/?id=mRNA-1647-P202

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Cytomegalovirus (CMV) Vaccine in Orthotopic Liver Transplant Candidates (COLT)

- **Study Design**: phase II study, randomized, double-blind, placebo-controlled, multi-center clinical trial in CMV seronegative prospective liver transplant recipients to determine the efficacy of two doses of CMV-MVA Triplex CMV vaccine pretransplant.
- **Primary objective**: To assess the effect of pre-Tx Triplex vaccination on duration of CMV antiviral therapy within the first 100 days post-Tx in CMV D+R- liver transplant recipients.
- A protocol-mandated preemptive therapy (PET) will be used for CMV disease prevention in D+R- LTxRs.
- **Status:** Open Summer/Fall 2024

Site PI: Erica Stohs, MD, MPH

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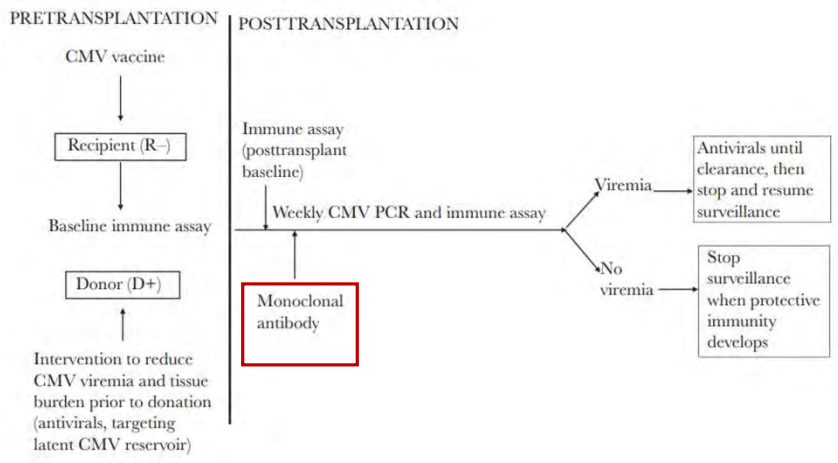
Monoclonal antibody



Haidar G *et al*. J Infect Dis. 2020 Mar 5; 221 (Suppl 1): S23-S31

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The LionHeart21 Study

- **Study design**: Phase 2, randomized, double-blind, placebo-controlled study of NPC-21 (Fiztasovimab) for kidney transplant recipients at high risk of CMV infection in the United States and Japan.
- **Administration:** IV infusion over approximately 60 min on Day 1 and at Week 4, 8, and 12 (Three arms: placebo, low dose (6 mg/kg) and high dose 12 mg/kg)
- **Primary Objective**: The incidence of CMV disease (CMV syndrome or tissue-invasive CMV disease) or CMV viremia (PCR analysis or antigenemia testing) by week 16.
- **Status:** Completed
- **Results:** NPC21 did not reduce the incidence of CMV disease and/or CMV viremia by week 16

Site PI: Diana Florescu, MD

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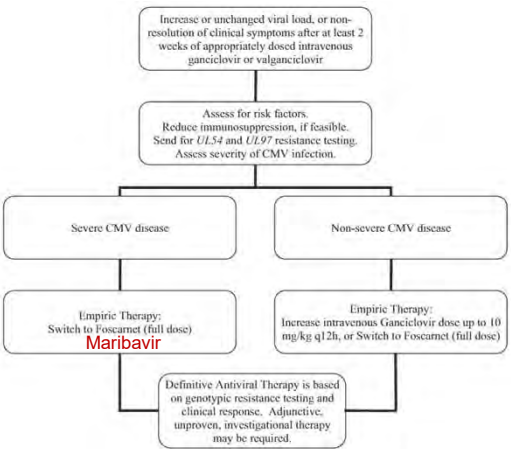
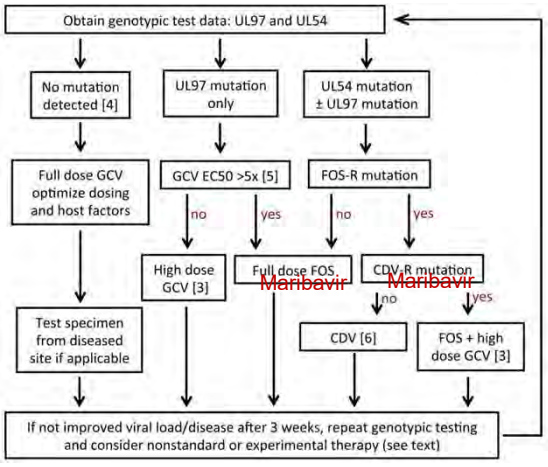
Post-Maribavir algorithm management





Slide Courtesy of Dr. Marcus Pereira

Razonable and Humar. *Clin Transplant*. 2019 Sep; 33(9):e13512
Kotton et al. Transplantation 2018;102:900-931

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Open-Label, single-arm study to evaluate safety and tolerability, pharmacokinetics, and antiviral activity of maribavir for the treatment of pediatric and adolescent transplant recipients with CMV infection

- **Study Design**: Phase 3, multicenter, open-label, single-arm, repeated-dose study
- **Primary Objectives**:
  - To characterize the pharmacokinetics of maribavir and identify dosing regimens for CMV infection treatment in pediatric HSCT and SOT subjects from 0 years to <18 years of age.
  - To assess the safety and tolerability of maribavir in children and adolescents.
- **Status**: Recruiting

Site PI: Natalia E. Castillo Almeida, MD

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RSV vaccines

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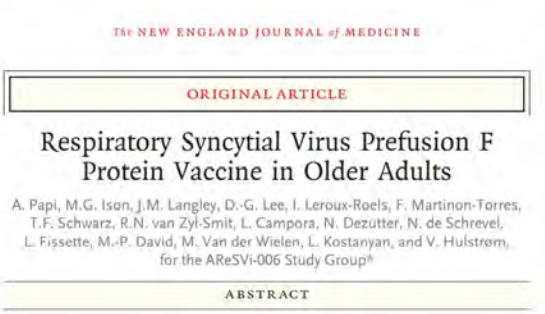
GSK RSV Vaccine Trial Takeaways

- Trial demonstrated safety and efficacy in preventing RSV-related LRTD in adults > 60 years of age
- Acceptable safety profile
- No data on effect of hospitalizations related to RSV LRTD
- Lower number of older adults > 80 years and more frail individuals
- Efficacy in immunocompromised remains unknown, IC excluded from study


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

A. Papi, M.G. Ison, J.M. Langley, D.-G. Lee, I. Leroux-Roels, F. Martinon-Torres, T.F. Schwarz, R.N. van Zyl-Smit, L. Campora, N. Dezutter, N. de Schrevel, L. Fissette, M.-P. David, M. Van der Wielen, L. Kostanyan, and V. Hulstrøm, for the AReSVi-006 Study Group*

ABSTRACT

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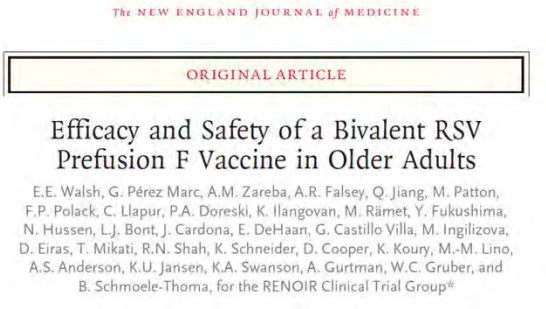
Pfizer RSV Vaccine Trial Takeaways

- Trial demonstrated safety and efficacy in associated LRTI and RSV-associated acute respiratory illness in adults > 60 years of age
- Acceptable safety profile
- No data on effect of hospitalizations related to RSV LRTD
- Immunocompromised excluded from study


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

E.E. Walsh, G. Pérez Marc, A.M. Zareba, A.R. Falsey, Q. Jiang, M. Patton, F.P. Polack, C. Llapur, P.A. Doreski, K. Ilangovan, M. Rämet, Y. Fukushima, N. Hussen, L.J. Bont, J. Cardona, E. DeHaan, G. Castillo Villa, M. Ingilizova, D. Eiras, T. Mikati, R.N. Shah, K. Schneider, D. Cooper, K. Koury, M.-M. Lino, A.S. Anderson, K.U. Jansen, K.A. Swanson, A. Gurtman, W.C. Gruber, and B. Schmoele-Thoma, for the RENOIR Clinical Trial Group*

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RSV Vaccines in Immunocompromised Hosts

Immunocompromised patients excluded from trials so vaccine efficacy in this population is unknown.

ACIP recommends RSV vaccine in immunocompromised adults under shared clinical decision-making given the potential for significant benefit.

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Clinical consideration: Shared clinical decision-making based on risk assessment among adults aged 60–64 years

For shared clinical decision-making recommendations there is no default.

The decision about whether or not to vaccinate an individual may be informed by:

- Best available evidence of who may benefit
- An individual's characteristics, values, and preferences
- Health care provider's clinical discretion
- Characteristics of the vaccine being considered

ACIP June 2023

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Clinical consideration: RSV vaccines and persons with immunocompromising conditions

Adults with immunocompromising conditions are at risk of severe RSV-associated disease and death.

They may benefit from RSV vaccination but were not included in the clinical trials so efficacy in this population is unknown.

These individuals, including those receiving immunosuppressive therapy, may have a diminished immune response to RSV vaccination.

Persons with immunocompromising conditions are recommended to receive the RSV vaccine under shared clinical decision-making given the potential for significant benefit.

ACIP June 202

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RSV vaccines in immunocompromised patients, what is on the horizon?

- A Study on the Immune Response and Safety of an RSV Vaccine When Given to Adults 18 Years of Age and Above Who Received ***Lung or Kidney Transplant*** and Are at an Increased Risk of Respiratory Syncytial Virus Lower Respiratory Tract Disease and Compared to Healthy Adults 50 Years of Age and Above (RSV OA=ADJ-023). **Status:** Active, not recruiting
- A Study to Assess the Safety, Tolerability, and Immunogenicity of RSVpreF in Adults at ***High Risk of Severe RSV Disease*** (MONET). **Status:** Active, not recruiting.

Site PI: Natalia E. Castillo Almeida, MD

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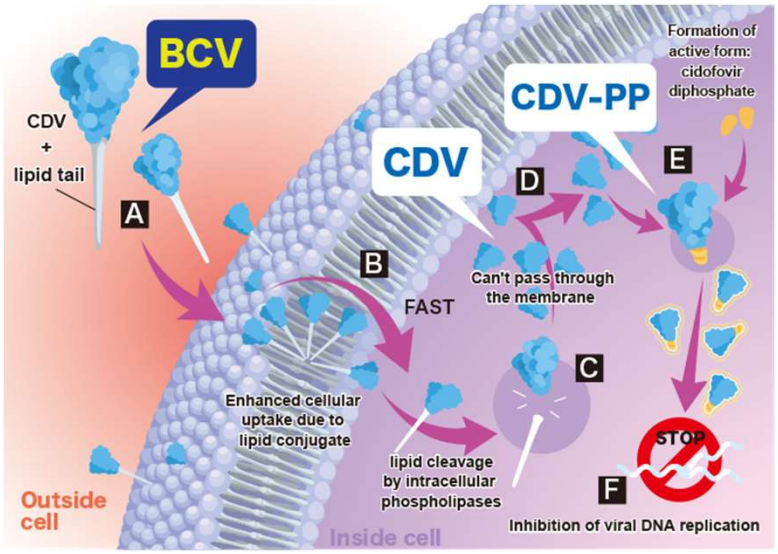

Brincidofovir

Image from symbiopharma.com

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ATHENA Trial

- **Study Design**: Phase IIa, Open label, multiple ascending dose confirmation study of the safety and tolerability of IV brincidofovir in adult and pediatric patients with adenovirus infection
- **Primary outcome:** treatment-related adverse events
- **Status:** Closed

Site PI: Carlos A. Gomez, MD

https://clinicaltrials.gov/ct2/show/NCT04706923

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Trial on Efficacy and Safety of Pritelivir Tablets for Treatment of Acyclovir-resistant Mucocutaneous HSV (Herpes Simplex Virus) Infections in Immunocompromised Subjects (PRIOH-1)

- **Study design:** Phase 3 randomized, open-label , multicenter, comparative trial
- **Intervention:** Pritelivir vs Investigator's choice (foscarnet, cidofovir, Imiquimod)
- **Primary outcome:** Efficacy measured by cure rate.
- **Status:** Active, recruiting

Site PI: Anum Abbas, MD

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Our team

florescuresearchteam@unmc.edu

Top row, left to right: Jacob (Jake) Williams, BA; Natasha (Tasha) Wilson APRN, FNP-C; Molly J. Ferris, BSN, RN; Rebecca (Becca) Cuthbert, MS; Matthew (Matt) E. Palmer, BSN RN CCRC
Bottom row, left to right: Spencer E. Caniglia; M. Grace Rodriguez, BSN, RN; Natalia E. Castillo Almeida, MD
Not pictured: Taylor Monahan, Allie M. Lewis and Kendra Stachum

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The future looks extremely bright indeed, with lots of possibilities ahead – big possibilities. Like the song says, We've just begun.
Bruce Lee
quotefancy

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