MTIS MIAMI TRANSPLANT INSTITUTE SYMPOSIUM 2026

What's New in Bugs and Drugs:
Pre-transplant optimization & Post-operative care and monitoring

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Disclosures

- No Conflicts of Interest to disclose
- I do not receive vaccine kickbacks

Common Infectious Diseases Myths

- Myth 1: Bug ≠ Drug
- Myth 2: Broad-spectrum antibiotics are more effective than narrow-spectrum ones
- Myth 3: Intravenous antibiotics are more effective than oral antibiotics
- Myt
- Myt
- Myt
- Myt
- Myth 8: Bactrim allergy/intolerance mandates alternative PJP prophylaxis
- Myth 9: Vaccines increase allograft rejection risk

Follow the Evidence

Challenging myths reduces antimicrobial toxicity and resistance while optimizing transplant outcomes

Pre-transplant optimization

- ID history & exam: Detailed infection, travel, TB, sexual, substance use, occupational, animal exposure, transfusion, prior transplant and vaccine history; focused exam for skin, catheters, dentition, chronic ulcers
- Serologies & Exposure specific screening
- Imaging and organ-specific tests: CXR, CT Chest, Urine Culture, Ascitic fluid Culture
- Vaccination optimization: Age and Seasonal appropriate vaccine recommended
- Treat active infections
- Pre-emptive/prophylaxis planning: Use serological data to guide, screen for MRSA, CRE, C.auris
- Education & counseling: Standard “safe living” counseling on hand hygiene, food/water safety, pets, soil exposures, travel, and sexual health; document caregiver teaching
- Deferral criteria (ID-driven): Uncontrolled sepsis or suspected deep-seated infection needing evaluation

Pre-transplant optimization

- Frailty and ID
- Vaccination
- Risk based screening: MRSA, MDROs, Candida auris
- Endemic infections screening: Chagas, Histoplasmosis

Frailty and Infection Risk

Key Assessment Tools

- **Fried Frailty Phenotype (FFP):** Based on five criteria: unintentional weight loss, exhaustion, low physical activity, weakness (grip strength), and slow gait speed; 3 or more indicates frailty.
- **Clinical Frailty Scale (CFS):** A 9-point scale describing function, from very fit (1) to terminally ill (9), often used in acute care for its simplicity and predictive power.
- **FRAIL Questionnaire:** A 5-item self-report tool (Fatigue, Resistance, Ambulation, Illnesses, Loss of weight) scoring 0-5 (Robust, Pre-frail, Frail).
- **Timed Up and Go (TUG) Test:** Measures mobility by timing how long it takes to stand up, walk a few steps, turn, and sit back down.
- **Liver Frailty Index (LFI)**: LFI >4.4 = high risk

Chart-based frailty assessments: Rockwood modified frailty index (mFI), Lekan frailty index (LFI), Charlston co-morbidity index (CCMI) score, and Karnofsky score

Frailty & Infection Risk by SOT Type

Organ	Study size	Frailty tool(s) used	Outcomes (rates and infection patterns)
Kidney	120–210 KT patients (prospective KTOP); 185,742 hospitalized KT recipients (HFRS analysis)	Fried phenotype / CFS; Hospital Frailty Risk Score (HFRS)	**In KTOP**, vulnerable/frail older candidates had **≈2-fold higher rates** of major infection events on the waitlist vs non-frail, predominantly UTI (~40–50%), respiratory infections (~25–30%), and skin/soft-tissue infections (~10–15%); these events were associated with more frequent/longer waitlist suspensions and more infection-related rehospitalizations post-KT. **In the HFRS cohort**, **severe infection** occurred in ~8–10% of low-frailty vs ~15–20% of moderate-frailty and **>25% of high-frailty hospitalizations**; high-risk HFRS conferred ≈3.2-fold higher odds of severe infection and higher in-hospital mortality and graft failure.
Liver	Several hundred cirrhosis and LT patients across multiple cohorts (pre- and post-LT)	Clinical Frailty Scale (CFS); Liver Frailty Index (LFI)	Frail candidates had ≈1.5–2-fold higher rates of infection-related hospitalizations pre-LT, with bacterial infections (SBP, pneumonia, UTI) accounting for ~60–70% of events. **After LT**, early (30–90 day) infectious complications occurred in **~35–45%** of frail vs ~20–25% of non-frail recipients, mainly intra-abdominal sepsis, catheter-related bloodstream infection, and bacterial pneumonia; invasive fungal infections (mainly Candida) comprised ~5–10% of events. These infections were associated with longer ICU stay, greater organ support, and higher short-term mortality in frail groups.

Lung	43 frail vs 43 non-frail LT recipients (post-LT case–control); additional 100+ thoracic candidates in prehab/frailty series	Short Physical Performance Battery (SPPB)–based frailty; CFS	**In the lung LT case–control cohort, any documented infection in the first post-LT year occurred in ≈60–70% of frail** vs 30–40% of non-frail recipients, mainly bacterial pneumonias, tracheobronchitis, and bloodstream infections (~20–25%), with fungal infections (Aspergillus/Candida) in ~10–15% and more frequent among frail patients. Thoracic series show frail candidates have ≈2-fold higher rates of infection-related admissions on the waitlist, largely lower respiratory tract infections and sepsis in the context of chronic respiratory support/devices, and **post-LT frailty remains linked to recurrent respiratory infections and ICU-level care.**

Kidney
1. Willicombe M, Dor FJF, et al. Frailty Impact on Kidney Transplantation in Older People. Transplantation. 2025.
2. Kapse B, et al. Hospital Frailty Risk Score predicts graft failure, severe infection and adverse discharge in hospitalized kidney transplant recipients. Sci Rep. 2025.
Liver
1. Marimuthu K, et al. Frailty and Infection in Solid-Organ Transplant Recipients. Transpl Infect Dis. 2025.
2. Lai JC, et al. Frailty as a determinant of liver transplant outcomes. Hepatology. 2025.
3. Sogbe M, et al. Frailty in liver transplantation: implications for perioperative outcomes. Liver Transpl. 2025.
4. Kim G, et al. The impact of age and frailty on hospitalization and survival in older patients with cirrhosis. Front Aging. 2025.
5. Association of Frailty With Clinical and Financial Outcomes Among Liver Transplant Recipients. Clin Transplant. 2024.
Lung
1. Singer JP, et al. Frailty in lung transplant recipients is associated with anemia and adverse outcomes. J Heart Lung Transplant (or equivalent thoracic journal). 2025.
2. Kotecha S, et al. Frailty Assessment and Candidate Optimization Before Thoracic Transplantation. Curr Opin Organ Transplant. 2026.
3. Wickerson L, et al. An innovative prehabilitation approach for lung transplant candidates. PM&R. 2025.

Clinical Implications: Frailty-Informed Strategy

Current Evidence and Gaps

- Only ~40% of transplant ID clinicians routinely assess frailty
- Practice varies; **no standardized guidelines** for immunosuppression adjustment
- Frailty-specific infection data (CMV, fungal, bacterial) remain sparse
- **Key gaps:** Organ-specific prophylaxis, optimal immunosuppression intensity

Consensus Recommendations

- Use validated tools at wait-listing (Abridged Phenotype, LFI, SPPB) for risk stratification
- Offer prehabilitation to all waitlisted candidates; exercise is safe & modifiable
- **Intensify infection surveillance in frail recipients; adjust prophylaxis by organ type & individual risk**
- Interdisciplinary care: transplant surgery, ID, geriatrics, PT/nutrition
- Post-transplant rehabilitation to combat frailty progression & improve long-term outcomes

Prevention: Vaccinations

- Annual Influenza, COVID-19 vaccine, RSV
- Hepatitis A & Hepatitis B (high dose in HD patients and non-responders)
- Pneumococcal vaccines : Prevnar-20
- *H. flu* and *N. meningitidis* (including serotype B) : Only in those with current or future anatomical/functional asplenia like multi-visceral transplant
- Zoster if VZV positive >50y
- Tdap if booster not given in last 10 years
- HPV Vaccine (9y – 45y)
- Varicella if VZV seronegative *live vaccine
- MMR if not immune *live vaccine
- Yellow fever, BCG, Oral Polio, Rotavirus *live vaccines

Live vaccines are contraindicated post-transplant!

Case#1 Vaccine decision making

68-year-old male with COPD listed for lung transplant comes to clinic in December for vaccine counselling. He is currently asymptomatic. What vaccines would you recommend for him?

A. Influenza, COVID-19, RSV now

B. Influenza, COVID-19, RSV after transplant, as he could get an offer at anytime

C. Vaccinate all household members

D. Influenza now, COVID-19 next week, RSV 2 weeks later

RSV Vaccine

FDA indications and age ranges

- RSVPreF3 (Arexvy, GSK): Single dose for in adults ≥60 years, adults 50–59 years at increased risk for severe RSV
- RSVPreF (Abrysvo, Pfizer): Single dose for adults ≥60 years; adults 18–59 years at increased risk, and maternal indication at 32–36 weeks' gestation to protect infants to 6 months
- mRNA-1345 (mRESVIA, Moderna): Approved for adults ≥60

Implications for practice

- For "standard-risk" older adults ≥60, all three are options; choice often hinges on supply, formulary, and shared decision-making about adjuvant vs mRNA platforms.
- For adults 18–59 at increased risk, only Abrysvo (RSVPreF); mRESVIA (mRNA-1345) approved 6/2025
- For pregnant patients, Abrysvo is uniquely indicated

Efficacy in high-risk groups: Immunocompromised excluded

Vaccine	Advanced Age (95% CI)		High-Risk Comorbidities (95% CI)		Immunocompromise
RSVpreF Efficacy against LRTD with ≥3 symptoms	≥75	= 85.7 (-11.2, 99.7)	• ≥1 comorbidity of interest* • ≥1 cardiorespiratory comorbidity†	• = 80.0% (40.3, 95.0) • = 72.7% (-3.2, 95.1)	Excluded from study
	≥80	= 100.0 (-51.5, 100.0)	• Pre-frail/frail	• = Not assessed	
RSVPreF3 Efficacy against LRTD (No adjustment by season)	≥75	= Not shared	• ≥1 comorbidity of interest** • ≥1 cardiorespiratory comorbidity†† • Pre-frail‡	• = 74.5% (55.7, 86.1) • = 80.1% (60.6, 91.0) • = 80.0% (57.3, 91.8)	Excluded from study
	≥80	= 52.6 (-64.2, 89.2)	• Frail‡‡	• = -116 (-12,800, 88.9)	
mRNA-1345 Efficacy against LRTD with ≥3 symptoms	Limited efficacy evidence No cases reported in vaccine or placebo groups for participants 80+		• Limited efficacy evidence: • ≥1 comorbidity of interest**	= 71.8% (95% CI: -35.9, 94.1)	Excluded from study

*COPD, asthma, diabetes mellitus, congestive heart failure, liver or renal disease
†COPD, asthma, congestive heart failure
‡Pre-frail defined by gait speed 0.4–0.99 m/s
‡‡Frail defined by gait speed <0.4 m/s or unable to complete assessment

**COPD, asthma, any chronic respiratory/pulmonary disease, diabetes mellitus, chronic heart failure, advanced liver or renal disease
††COPD, asthma, any chronic respiratory/pulmonary disease, chronic heart failure

Melgar M & Britton A. Evidence to Recommendations Framework Respiratory Syncytial Virus (RSV) in Adults [Presentation slides]. Presented at the ACIP meeting, Atlanta, GA; 6/21/23. f.
Wilson E, et al. 7th ReSV iNET Conference (RSVVW 2023); Lisbon, Portugal. Abstract 123.
Papi A, et al. N Engl J Med. 2023;388(7):595-608. Walsh EE, et al. N Engl J Med. 2023;388(16):1465-1477.
Melgar M, et al. MMWR. 2023 / 72(29);793-801.

RSV Vaccines in SOT and HCT recipients

Population	Vaccine(s) Studied	Key Findings	References
Allogeneic HCT recipients	Prefusion F–based RSV vaccines	- Significant rise in anti–pre-F IgG titers at 4 and 12 weeks post-vaccination. - Lower baseline IgG among those on recent systemic immunosuppression. - Some patients required a second dose due to inadequate early response. - Neutralizing antibody titers strongly correlated with pre-F IgG levels (r = 0.916).	**Redjoul et al., 2025 (JAMA Network Open)**
Solid organ transplant recipients (mixed organs)	RSVPreF3 RSVpreF	- Prefusion F IgG ↑ ~5.5-fold at 4 weeks. - 67% achieved ≥4-fold IgG rise at 4 weeks; 52% reached high-titer response by 4 weeks (62% RSVPreF3 vs 25% RSVpreF). - Response persisted at week 12 with some decline.	**Karaba et al., 2025 (OFID)**
Solid organ transplant recipients (Phase III trial)	mRNA-1345	- Safety profile similar to the general population. - Strong RSV-A and RSV-B neutralizing antibody GMT increases after two-dose regimen. - Adverse events mostly grade 1–2 and self-limited.	**Mayer et al., 2025 (IDWeek)**
Lung & allogeneic HCT recipients (RSVax trial—ongoing)	RSVPreF3	- Trial evaluating humoral + cellular immunity at 4 weeks, 6 months, and 12 months. - Results pending.	**Hall et al., 2025 (ClinicalTrials.gov)**

- Robust immunogenicity is observed in both HCT and SOT recipients, though responses are attenuated compared with immunocompetent adults.
- RSVPreF3 may produce slightly stronger prefusion-F antibody responses than RSVPreF in SOT cohorts
- Immunosuppression level (recent steroids, calcineurin inhibitors, lymphocyte counts) influences antibody responses.
- Clinical efficacy data (i.e., reduction in RSV infection/hospitalization) remain insufficient; current evidence is primarily immunogenicity data.
- Safety profiles across SOT and HCT recipients appear acceptable, with mostly mild, self-limited reactions.

IDSA Recommendations for RSV vaccination

- **In adults and adolescents with compromised immunity*, the IDSA guideline panel recommends administering age-appropriate RSV vaccinations (*strong recommendation, moderate certainty of evidence*)**

- For immunocompromised patients <18 years, administration should be guided by shared decision making
- Solid organ transplant candidates, especially lung transplant, should ideally be vaccinated pre-transplant
- Household members and close contacts of immunocompromised patients should be up to date with RSV vaccination, if eligible
- It is appropriate for patients to receive COVID-19, influenza, and RSV vaccines together

RSV Vaccination Guidance: Timing of Vaccine

Group	Suggested timing of RSV vaccine*, **
Solid organ transplant	• At least 2 weeks pre-SOT; or ≥6 months post-SOT. Can be given as early as 1 month after transplant during RSV season
Hematologic malignancy	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 6 months after last infusion ○ For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HCT/CAR-T	• Optimal timing includes ≥6 months after transplant or CAR-T treatment ○ For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
Solid tumor chemotherapy	• At least 2 weeks before starting therapy; during/after is acceptable
Primary Immuno-deficiency	• Align with IVIG/SCIG or clinic access
Autoimmune immunosuppression	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3-6 months after last infusion ○ For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HIV	• Align with preventive routine care

*Defer during acute transplant rejection treatment or severe/acute illness

**Use shared-decision making for early windows based on levels of community virus circulation

RSV mAbs: Clinical trial results in infants

NIRSEVIMAB

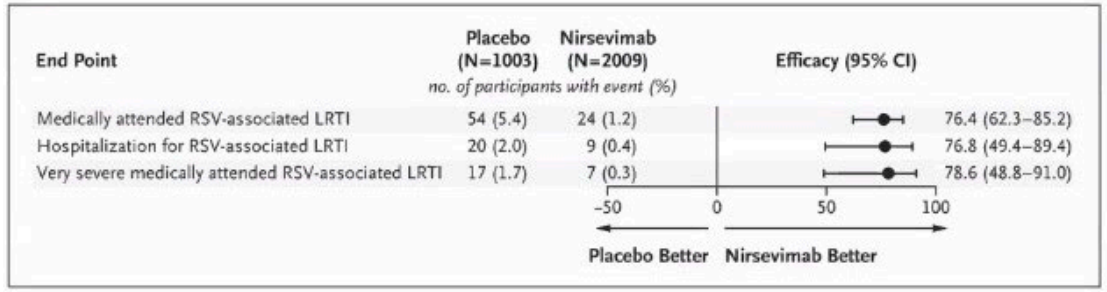
- Preterm, late preterm, and healthy infants evaluated in randomized placebo controlled trials
- Pooled analysis: 79.5% relative risk reduction for medically attended RSV LRTI

CLESROVIMAB

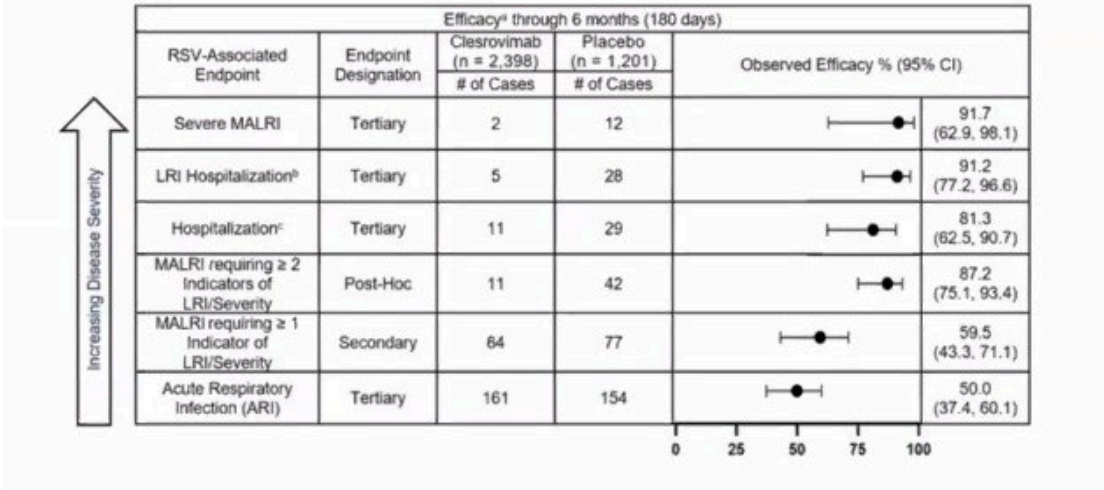
- Similar trial design
- Efficacy against medically attended RSV LRTI: 91.2%

Studies in immunocompromised hosts needed

- Important considerations include dosing, development of resistance, endpoints



End Point	Placebo (N=1003)	Nirsevimab (N=2009)	Efficacy (95% CI)
	no. of participants with event (%)		
Medically attended RSV-associated LRTI	54 (5.4)	24 (1.2)	76.4 (62.3–85.2)
Hospitalization for RSV-associated LRTI	20 (2.0)	9 (0.4)	76.8 (49.4–89.4)
Very severe medically attended RSV-associated LRTI	17 (1.7)	7 (0.3)	78.6 (48.8–91.0)



RSV-Associated Endpoint	Endpoint Designation	Clesrovimab (n = 2,398) # of Cases	Placebo (n = 1,201) # of Cases	Observed Efficacy % (95% CI)
Severe MALRI	Tertiary	2	12	91.7 (62.9, 98.1)
LRI Hospitalization[b]	Tertiary	5	28	91.2 (77.2, 96.6)
Hospitalization[c]	Tertiary	11	29	81.3 (62.5, 90.7)
MALRI requiring ≥ 2 Indicators of LRI/Severity	Post-Hoc	11	42	87.2 (75.1, 93.4)
MALRI requiring ≥ 1 Indicator of LRI/Severity	Secondary	64	77	59.5 (43.3, 71.1)
Acute Respiratory Infection (ARI)	Tertiary	161	154	50.0 (37.4, 60.1)

Efficacy[a] through 6 months (180 days)

Griffin, NEJM 2020
Hammitt, NEJM 2022
Muller, NEJM 2023
Simoes, Lancet Child Adol Health 2023

Resources for Vaccine Guidance

- IDSA Guidelines
- American Academy of Pediatrics
- CDC/ACIP data undergoing revision

Risk-based infectious screening

- MRSA, VRE, MDROs
- Candida auris
- Endemic infections

MRSA & MDROs

Who Gets Screened for MRSA and MDROs?

- Hospital Admissions: Universal or targeted screenings on admission
- High-Risk Units/ Intensive Care Units (ICUs)
- Transfer Patients: From other healthcare facilities, long-term care or nursing homes
- Prior History: Patients with a known hx of MRSA or other MDRO colonization or infection.
- Pre-Surgery
- Outbreak Situations

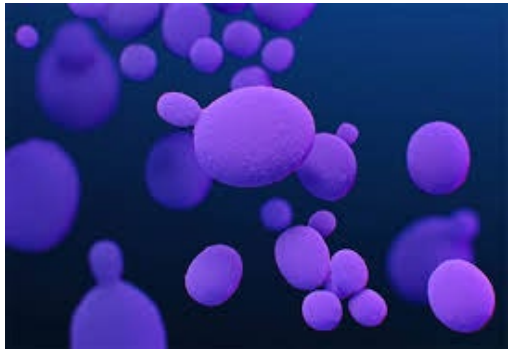
How Screening is Performed

- **Nasal Swab:** The most common method for MRSA.
- **Wound/Skin Swab:** If open sores are present.
- **Rectal/Groin Swabs:** Often used to detect Gram-negative MDROs.

Why is it needed?

- Identify those carrying the bacteria without symptoms and implement contact precautions to protect other patients
- Tailor peri-operative antibiotic prophylaxis accordingly

Candida (Candidozyma) auris



- Candida auris is an emerging, multidrug-resistant yeast

- Overall risk of progression from colonization to invasive *C. auris* infection was approximately 2% over 12 months; 18% to 25% in critically ill especially mechanically ventilated patients

- Risk factors for Candida auris: epidemiologic exposure, ICU stay, invasive devices, repeated healthcare encounters, exposure to antibiotics

- **Screening Gap**: There are no transplant-specific, standardized national recommendations in the U.S. for routine perioperative screening of SOT donors or recipients

D. J. Sexton, M. L. Bentz, R. M. Welsh, et al., "Positive Correlation Between Candida auris Skin-Colonization Burden and Environmen-tal Contamination at a Ventilator-Capable Skilled Nursing Facility in Chicago," Clinical Infectious Diseases 73, no. 7 (2021): 1142–114

Received: 27 March 2020 | Revised: 5 June 2020 | Accepted: 6 June 2020
DOI: 10.1111/ajt.16144

CASE REPORT

AJT

Candida auris outbreak involving liver transplant recipients in a surgical intensive care unit

- Cluster of 5 Liver tx patients in one ICU infected or colonized
- All isolates azole resistant
- 2 Patients died

Received: 29 April 2022 | Revised: 10 June 2022 | Accepted: 17 June 2022
DOI: 10.1111/tid.13919

ORIGINAL ARTICLE

Challenges and opportunities in stewardship among solid organ transplant recipients with *Candida auris* bloodstream infections

Christine A. Vu[1] | Adriana Jimenez[2,3] | Shweta Anjan[4,5] | Lilian M. Abbo[2,4,5]

- 5 SOTr developed *C.auris* infections
- Median time: 43 days from hospital admission
- One patient died

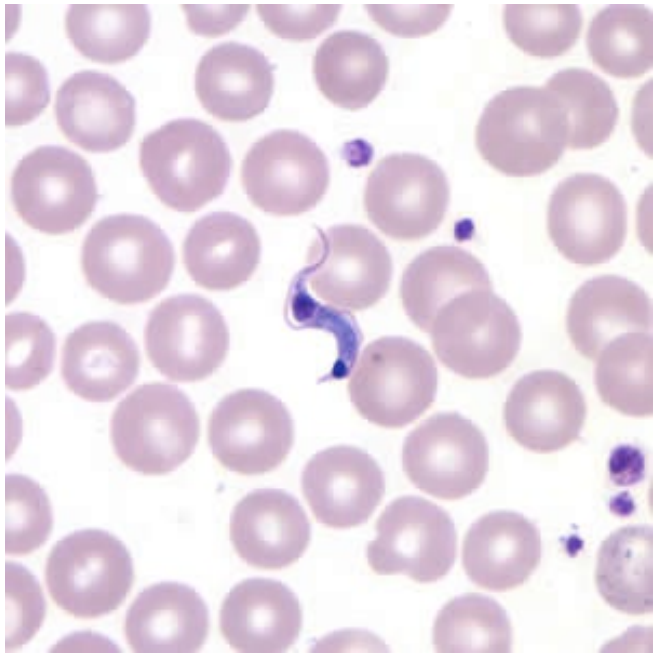
Endemic infections: Chagas

- Born or lived in endemic region
- Mother at risk for Chagas
- Received blood transfusion in endemic region
- Prior history of Chagas
- Test: Chagas Serology, followed by confirmatory PCR if positive

Table 2: Countries with endemic Chagas disease[1,2]

Argentina
Belize
Bolivia
Brazil
Chile
Colombia
Costa Rica
Ecuador
El Salvador
French Guiana
Guatemala
Guyana
Honduras
Mexico
Nicaragua
Panama
Suriname
Paraguay
Peru
Uruguay
Venezuela

Endemic infections: Chagas



- Infection occurs via exposure to parasite *Trypanosoma cruzi*, transmitted by triatomine (“kissing”) bugs
- **Clinical presentation:** Acute infection is often mild or asymptomatic, while chronic disease may cause cardiomyopathy, arrhythmias, or gastrointestinal dysmotility
- **Diagnosis:** Diagnosis relies on **two distinct serologic assays** for chronic infection; PCR is useful in acute disease or reactivation
- **Treatment:** Benznidazole or nifurtimox for acute infection or reactivation

PLOS Neglected Tropical Diseases

RESEARCH ARTICLE

Field evidence of *Trypanosoma cruzi* infection, diverse host use and invasion of human dwellings by the Chagas disease vector in Florida, USA

Norman L. Beatty[1,2e*], Chanakya R. Bhosale[3,4e], Zoe S. White[3], Carson W. Torhorst[3], Kristen N. Wilson[3], Rayann Dorleans[3], Tanise M.S. Stenn[5], Keswick C. Killets[6], Rachel Curtis-Robles[6], Nathan Burkett-Cadena[5], Eva Nováková[7], Gabriel L. Hamer[8], Sarah A. Hamer[6], Samantha M. Wisely[2,3]

- From 2013-2023, utilizing field work and community science programs, 310 triatomines from various regions in Florida.
- Both adult and immature triatomines were found, and about one-third of the triatomines were found inside human homes (35%).
- About 30% of the triatomines tested were infected with the Chagas disease parasite, *Trypanosoma cruzi*.
- Raises concerns for possible transmission of Chagas disease to humans from triatomines in Florida

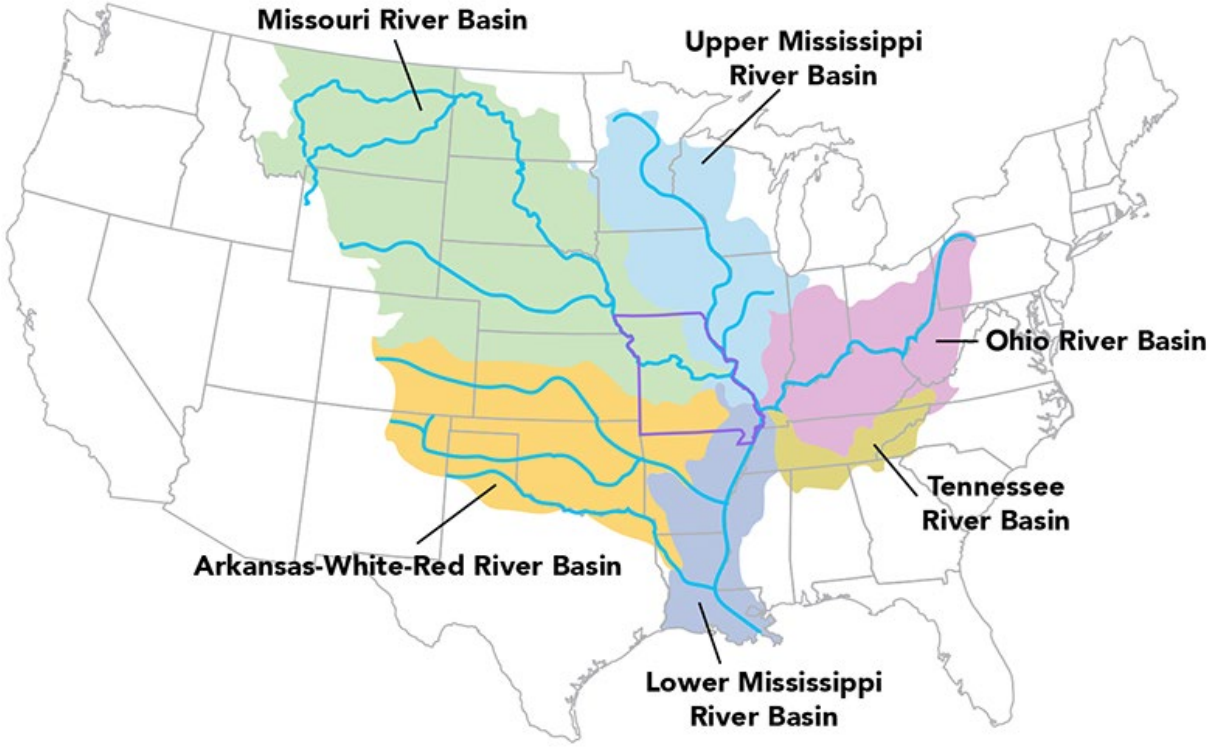
Case #2

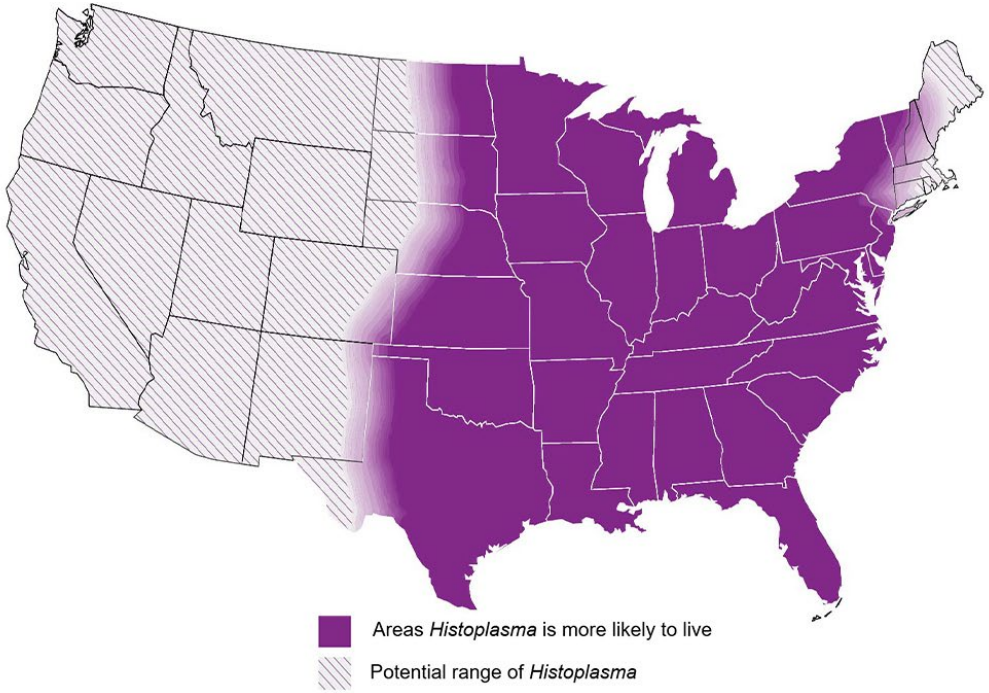
A recent outbreak of a fungal infection in the United States has been primarily reported in which state?

A. Arizona
B. Tennessee
C. New Mexico
D. Florida

The New York Times

Dozens Are Sickened by a Fungal Infection in Tennessee





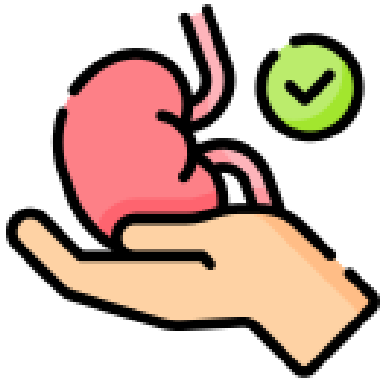
Endemic infections: Histoplasmosis

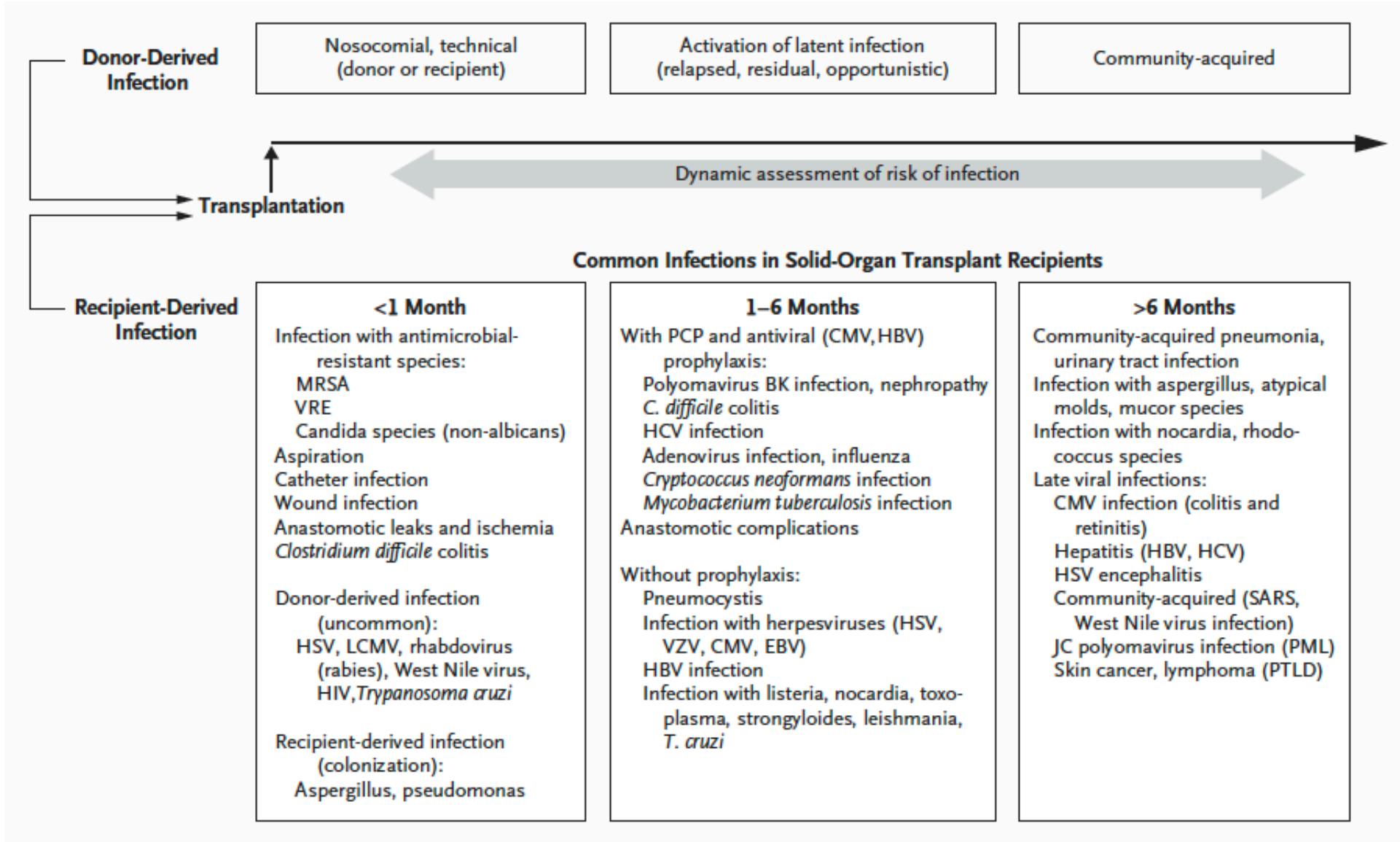
- **Source:** Infection follows inhalation of spores from soil contaminated with bird or bat droppings (e.g., caves, construction, demolition)
- **Clinical presentation:** Ranges from asymptomatic or mild pulmonary disease to severe disseminated infection in immunocompromised hosts
- **Diagnosis: Urine Histoplasma antigen testing** is the most sensitive and rapid diagnostic test
- **Treatment:** Mild disease may be self-limited, while moderate–severe disease requires itraconazole or amphotericin B depending on severity and host factors

Pre-Transplant Optimization: Summary

- Screen
- Vaccinate
- Treat/mitigate
- Prophylaxis plan

POST-OP CARE & MONITORING





Timeline of Infections Post-Transplant

Fishman JA. Infection in solid-organ transplant recipients. *N Engl J Med*. 2007

Case #3 Donor history to worry about

You are evaluating an organ donor for a potential liver transplant candidate. What history would be a cause for concern?

A. 40-year-old homeless male, sustained severe injuries in a motor vehicle accident
B. 65-year-old female with an intracranial hemorrhage
C. 59-year-old female, sustained a cardiac arrest, recently bitten by his pet dog
D. 55-year-old male, sustained traumatic injury, required massive blood transfusion protocol

Donor-derived infections: New bugs reported

When to suspect

Timing: Within first month post-transplant (can be as long as 4-5 months post)

Multiple recipients: Infections from same donor affecting multiple organ recipients

Unusual pathogens: Endemic fungi, TB, parasites, uncommon bacteria/viruses

High-risk donors: Bacteremia, untreated infections, high-risk behaviors, endemic exposures

U.S. Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 74 / No. 39
December 4, 2025

Human-to-Human Rabies Transmission via Solid Organ Transplantation from a Donor with Undiagnosed Rabies — United States, October 2024–February 2025

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Rabies recap –

1. Rabies virus can be transmitted via direct contact of saliva, tears, or tissues (e.g., organs and other body tissues) from infected humans or animals with broken skin or mucous membrane
2. The rabies incubation period is often weeks to months
3. Animal reservoirs: bats, raccoons, skunks, and foxes
4. PEP consists of human rabies immunoglobulin and 4 rabies vaccine doses

- *If a potential donor, particularly one with acute encephalopathy, had a bite or scratch from a rabies-susceptible animal during the preceding year, transplant teams should consider consulting public health officials/CDC to determine rabies risk*

Bartonella quintana infection in kidney transplant recipients from donor experiencing homelessness, United States, 2022

Donor-derived bartonellosis in solid organ transplant recipients from unhoused donors in Alberta

Dima Kabbani [1,*], Efrat Orenbuch-Harroch [1], Carl Boodman [2], Sarah Broad [3], Manuel Paz-Infanzon [1], Sara Belga [4], Oscar A. Fernández-García [1], Emily Christie [5], Majid L.N. Sikosana [5], Soroush Shojai [5], Sita Gourishankar [5], Carlos Cervera [1], Karen Doucette [1]

- *Bartonella quintana* is a small, intracellular, gram-negative bacillus that can cause severe disease such as endocarditis, chronic bacteremia, and a severe vasoproliferative disease in the skin and visceral organs known as bacillary angiomatosis
- Treatment: Doxycycline +/- Azithromycin
- Transmission to humans occurs through an infected human body louse (Pediculus humanus corporis) and is, therefore, associated with poorly hygienic and crowded environments
- During World War I, it was known as trench fever, but it has been associated with urban homelessness more recently
- An investigation of the donor was significant for a history of alcohol use disorder, traumatic brain injury that led to brain death despite neurosurgical interventions, as well as a history of unsheltered homelessness in the months before the terminal hospitalization
- Transplant providers should consider Bartonella infection in the appropriate clinical setting

Transmission of yellow fever vaccine virus through blood transfusion and organ transplantation in the USA in 2021: report of an investigation

*Carolyn V Gould, Rebecca J Free, Julu Bhatnagar, Raymond A Soto, Tricia L Royer, Warren R Maley, Sean Moss, Matthew A Berk, Rebecca Craig-Schapiro, Rosy Priya L Kodiyanplakkal, Lars F Westblade, Thangamani Muthukumar, Yoram A Puius, Amresh Raina, Azam Hadi, Kymberly A Gyure, Danielle Trief, Marcus Pereira, Matthew J Kuehnert, Vennus Ballen, Debra A Kessler, Kimberly Dailey, Charles Omura, Thuy Doan, Steve Miller, Michael R Wilson, Jennifer A Lehman, Jana M Ritter, Elizabeth Lee, Luciana Silva-Flannery, Sarah Reagan-Steiner, Jason O Velez, Janeen J Laven, Kelly A Fitzpatrick, Amanda Panella, Emily H Davis, Holly R Hughes, Aaron C Brault, Kirsten St George, Amy B Dean, Joel Ackelsberg, Sridhar V Basavaraju, Charles Y Chiu, J Erin Staples, and the Yellow Fever Vaccine Virus Transplant and Transfusion Investigation Team**

- Four patients who had received a SOT in NE-USA developed encephalitis 2–6 weeks after transplantation
- On Investigation, 3 days before organ procurement, the organ donor received a blood transfusion from a donor who had received a yellow fever vaccine 6 days before blood donation
- Health-care workers providing vaccinations should inform patients of the need to defer blood donation for at least 2 weeks after receiving a yellow fever vaccine
- Blood banks in the United States screen donated blood for HIV types 1 and 2, hepatitis B (HBV), hepatitis C (HCV), human T-cell lymphotropic virus (HTLV) types I and II, syphilis, West Nile virus, Chagas disease, and Zika virus

Case #4 Treating Influenza

A 58-year-old man with end-stage kidney disease due to diabetic nephropathy underwent a deceased-donor kidney transplant 18 months ago. He presents in January with 2 days of fever, myalgias, headache, sore throat, and dry cough. He denies shortness of breath or chest pain.

A nasopharyngeal PCR panel is positive for **Influenza A.**

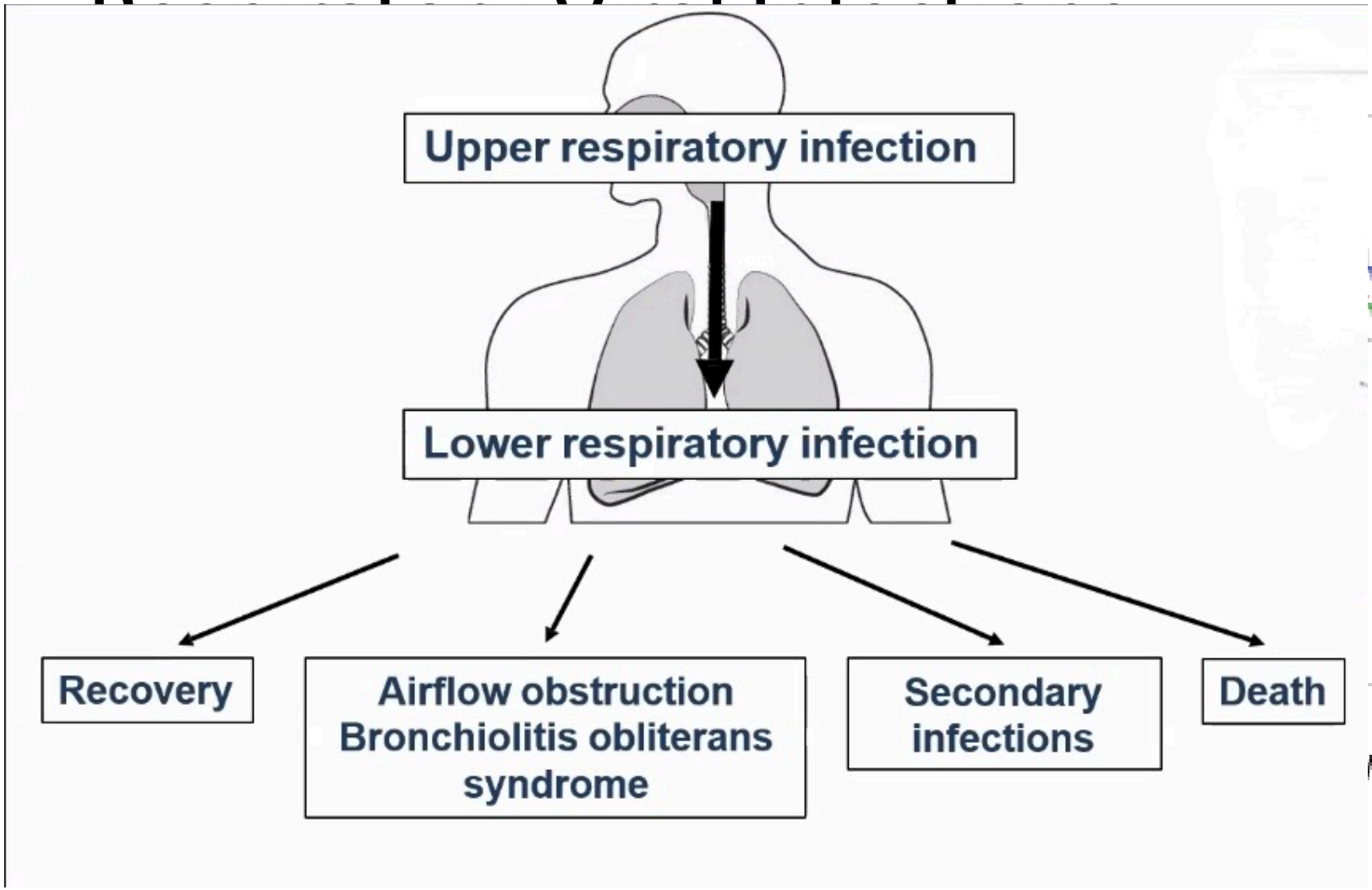
Which of the following is the most appropriate treatment for this patient?

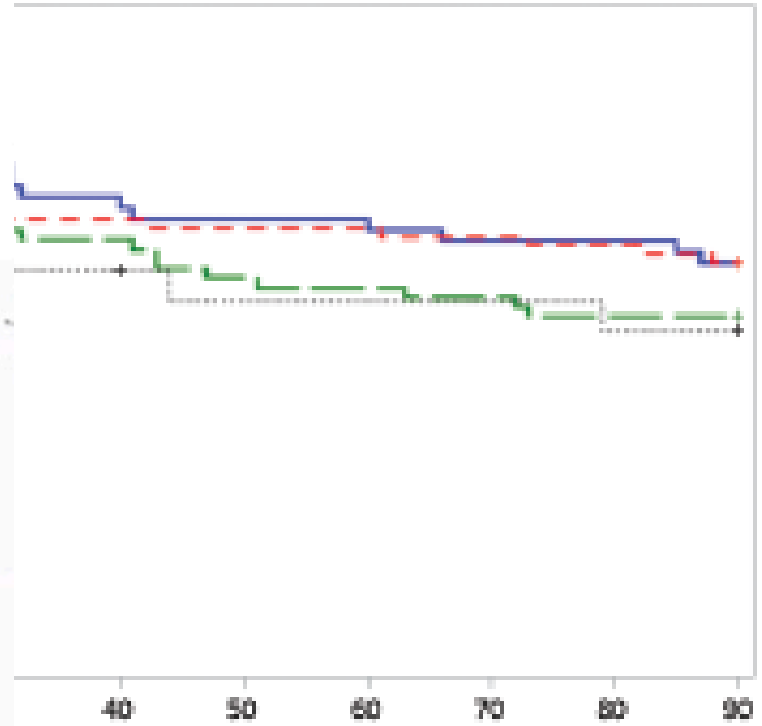
A. Oseltamivir

B. Zanamivir

C. Peramivir

D. Baloxavir marboxil





s after diagnosis

Influenza

JAMA Published online December 18, 2025

PERSPECTIVE

Influenza A(H3N2) Subclade K Virus
Threat and Response

Maria Zambon, BSc, BM, BCh, PhD; Frederick G. Hayden, MD

Vaccine efficacy of 30-40% in adults

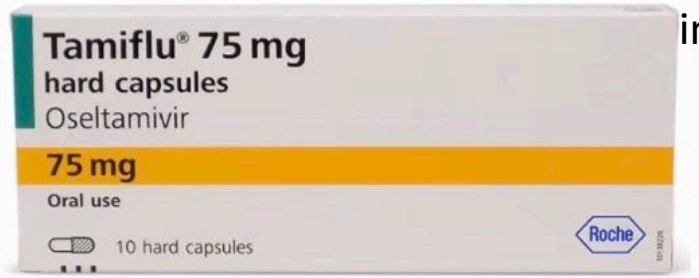
Little data on severity and risk of complications – 2025/26 season considered having "high severity" in children and "moderate severity" in adults

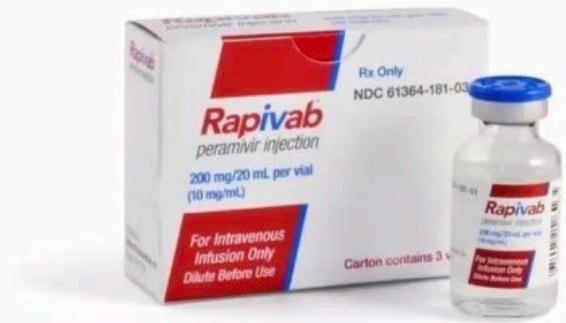
No concern so far on antiviral resistance

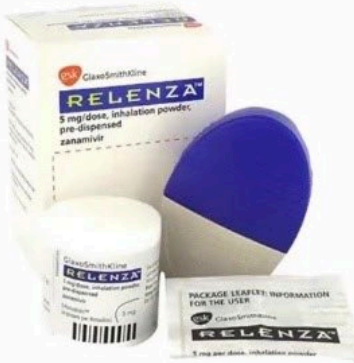
No data on immunocompromised patients

Baloxavir marboxil (oral, single dose)
Approved for uncomplicated influenza
Limited data in solid organ transplant recipients
Resistance can emerge, especially in immunocompromised hosts
Not first-line

Oseltamivir (oral)
Preferred in solid organ transplant recipients
Requires **renal dose adjustment**
Most clinical experience in immunocompromised hosts







Zanamivir (inhaled)
Avoid in patients with asthma or COPD
Not ideal in severe illness or hospitalized patients

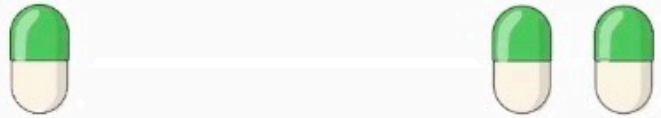
Peramivir (intravenous)
Used in hospitalized or severe cases
Requires renal dose adjustment

Infect Dis Ther (2019) 8:613–626
https://doi.org/10.1007/s40121-019-00271-8

ORIGINAL RESEARCH

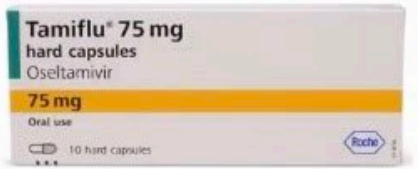
Safety, Resistance, and Efficacy Results from a Phase IIIb Study of Conventional- and Double-Dose Oseltamivir Regimens for Treatment of Influenza in Immunocompromised Patients

Essack Mitha · Gergely Krivan · Frederique Jacobs · Arnon Nagler · Sally Alrabaa · Analia Mykietiuk · Andrew Kenwright · Sophie Le Pogam · Barry Clinch · Loreta Vareikiene

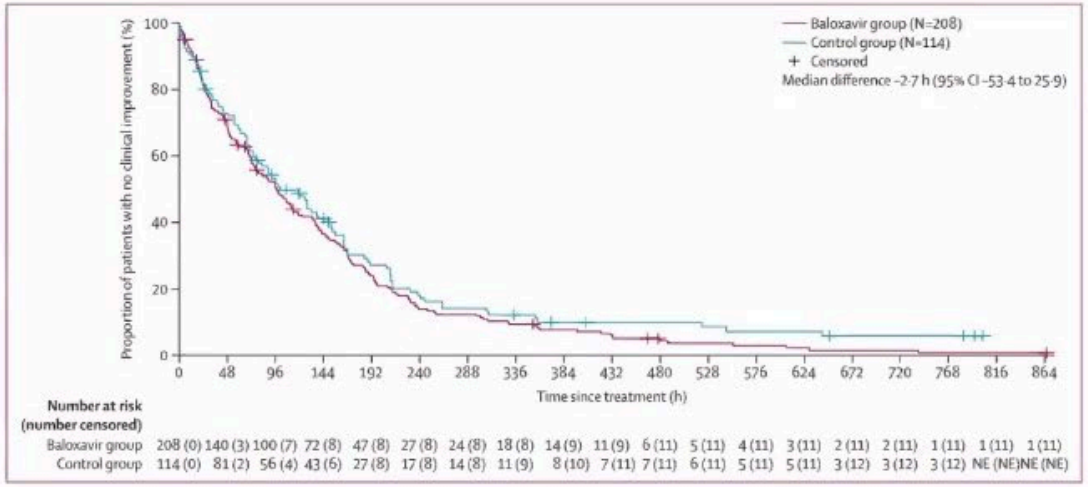


	n=105	n=110
Admission	6.8%	7.7%
Viral load decline	- 3.5 log10 vp/ mL	- 3.0 log10 vp/mL
Median time of shedding	178 h (152-227)	155 h (134-221)
Antiviral resistance	**12/73 (16%)**	**3/79 (4%)**
AE	50%	59%

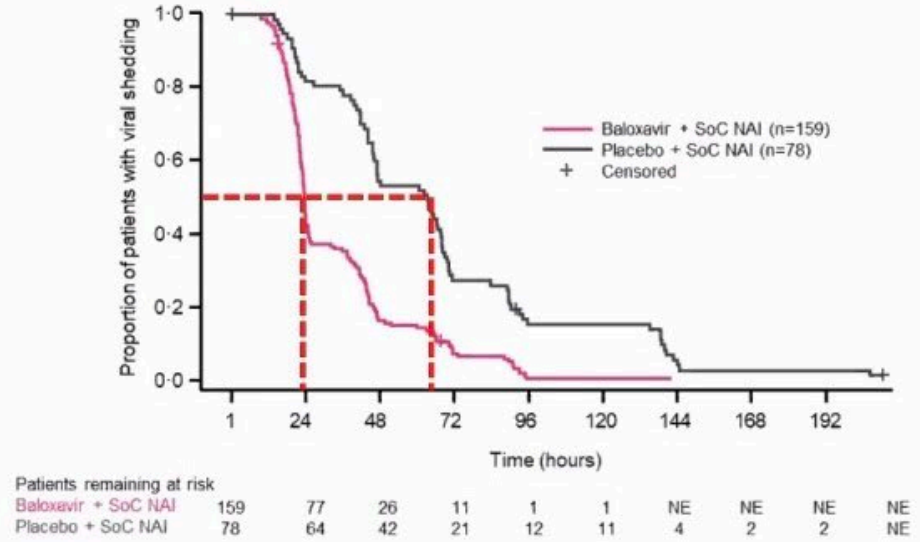
Role of double-dose Tamiflu



Clinical improvement
Primary outcome



Viral shedding
Secondary outcome



Kumar D et al. Lancet Infect Dis 2022

Role of combination therapy: Decreased viral shedding by ~2days

Influenza Summary

- Limited evidence on antiviral treatment and prevention of Influenza in individuals with immunosuppression
- Baloxavir, faster reduction of viral load but higher potential risk of resistance
- Higher doses, prolonged therapy, combination therapy: restricted to high-risk patients (HSCT, lung transplantation, ICU admission)
- Post exposure prophylaxis with Oseltamivir is ~80% effective

Parainfluenza

- Up to 13-40% of lower respiratory tract infections (LRTI) in children
- 90% seropositivity in adults but reinfection common

- HSCT:
  - Incidence of 4-7% with progression to LRTI in 13-43%; Mortality 12-50%
  - Up to 17.9 times greater odds of airflow decline post-infection

- Lung Transplant:
  - Incidence: 2-5%
  - Can lead to Chronic Lung Allograft Dysfunction/Bronchiolitis Obliterans (CLAD/BOS)

Management – Limited

- **DAS181 (Phase II RCT, NCT01644877)**

- **Ribavirin (aerosolized, oral, IV)**
  - Data limited to small case reports and series, some benefit, but significant heterogeneity in the individual studies
  - HSCT: 31/55 PIV-infected HSCT recipients received aerosolized ribavirin +/- Intravenous immunoglobulin
  - Treatment not associated with reduction in viral shedding or mortality
  - Lung Transplant: conflicting evidence regarding ribavirin and prevention of CLAD/BOS

RSV (respiratory syncytial virus)- Management

Ribavirin

Efficacy data primarily based on retrospective studies

Aerosolized

- HCT: Most evidence for efficacy against progression; some evidence of mortality benefit
- SOT: Most data for benefit in lung transplant recipients Expensive and difficult to administer
- Teratogenic effects
- Claustrophobia, bronchospasm, nausea, conjunctivitis

Oral

- HCT: Smaller studies have demonstrated benefit
- SOT: Smaller studies in lung transplant recipients
- Easier to administer
- Hemolysis, abnormal liver function tests, drug-drug interactions, renal function

Intravenous

In US, available by eIND only

Case#5 CMV Resistance? Refractory? Some other R?

- 55-year-old underwent deceased-donor kidney transplant for diabetic nephropathy. Induction with Thymoglobulin. Maintenance tacrolimus, mycophenolate and prednisone.

- Acute cellular rejection at one month.

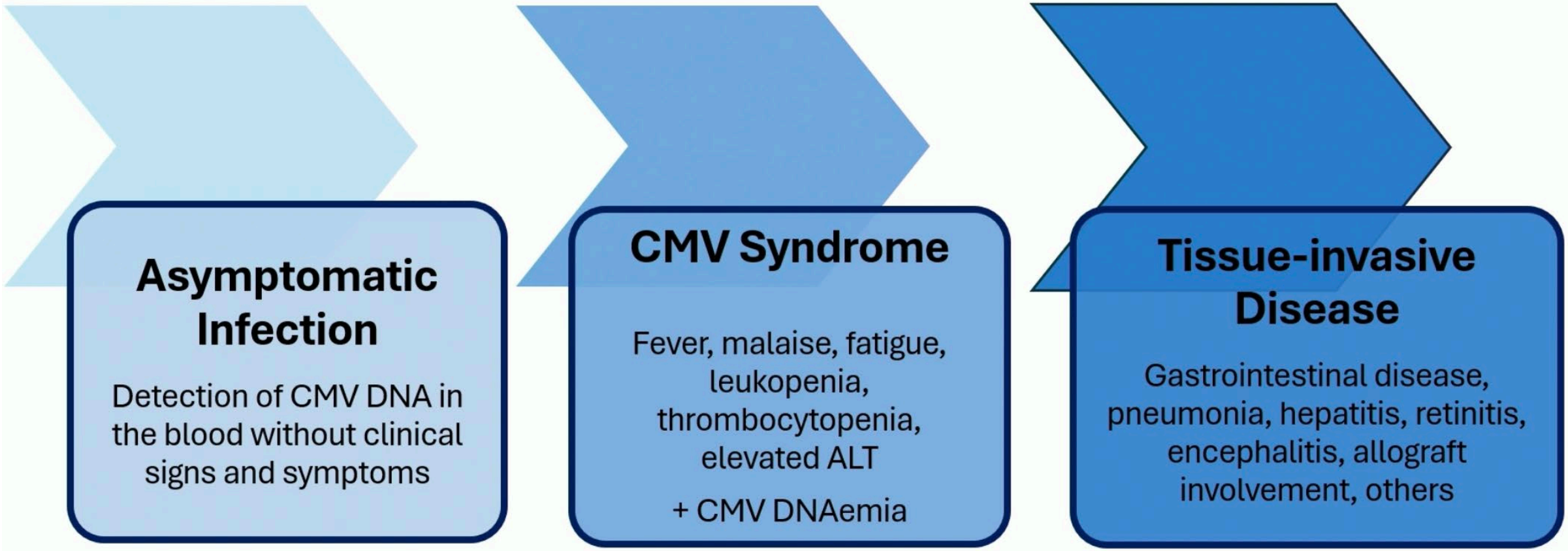
- CMV D+/R- mismatch: valganciclovir prophylaxis for 6 months

- 8 months after transplant: fever, malaise, diarrhea for 2 weeks.

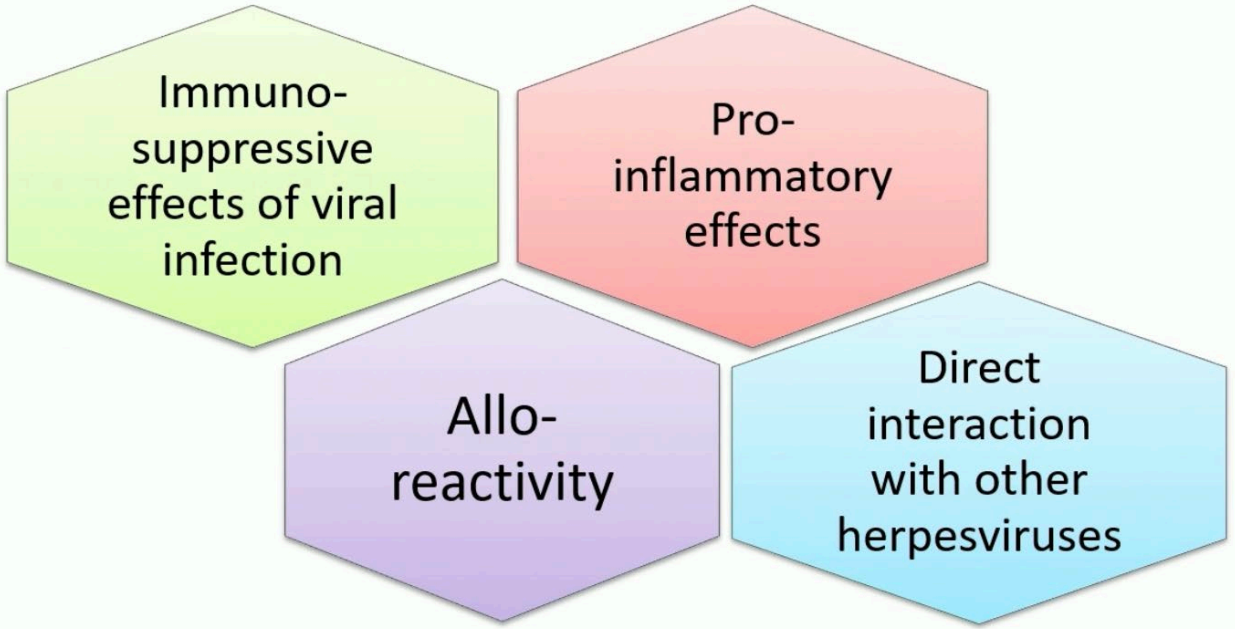
- CMV PCR: 975,000 IU/ml of plasma

- Colonoscopy was refused

CMV Infection and Disease



Indirect Effects of CMV



Opportunistic infections:

- Bacterial fungal superinfection
- Graft rejection; graft dysfunction
- Decreased graft and patient survival
- Herpesvirus interactions: EBV/PTLD

Available Antiviral Drugs

Antiviral Drugs	BONE MARROW	KIDNEY	GASTRO INTESTINAL	ELECTRO LYTES
Ganciclovir IV/valganciclovir PO (*UL54 CMV DNA polymerase inhibitor*)	✓ NEUTROPENIA LEUKOPENIA			
Foscarnet (*UL54 CMV DNA polymerase inhibitor*)		✓ RENAL FAILURE		✓ Ca, Mg, K, Phos
Cidofovir (*UL54 CMV DNA polymerase inhibitor*)		✓ RENAL FAILURE		
Letermovir (CMV prophylaxis only) (*UL56 viral terminase inhibitor*)			✓ NAUSEA	
Maribavir (refractory/resistant CMV treatment) (*UL97 kinase inhibitor*)			✓ DYSGEUSIA	

Treatment of CMV Disease in SOT

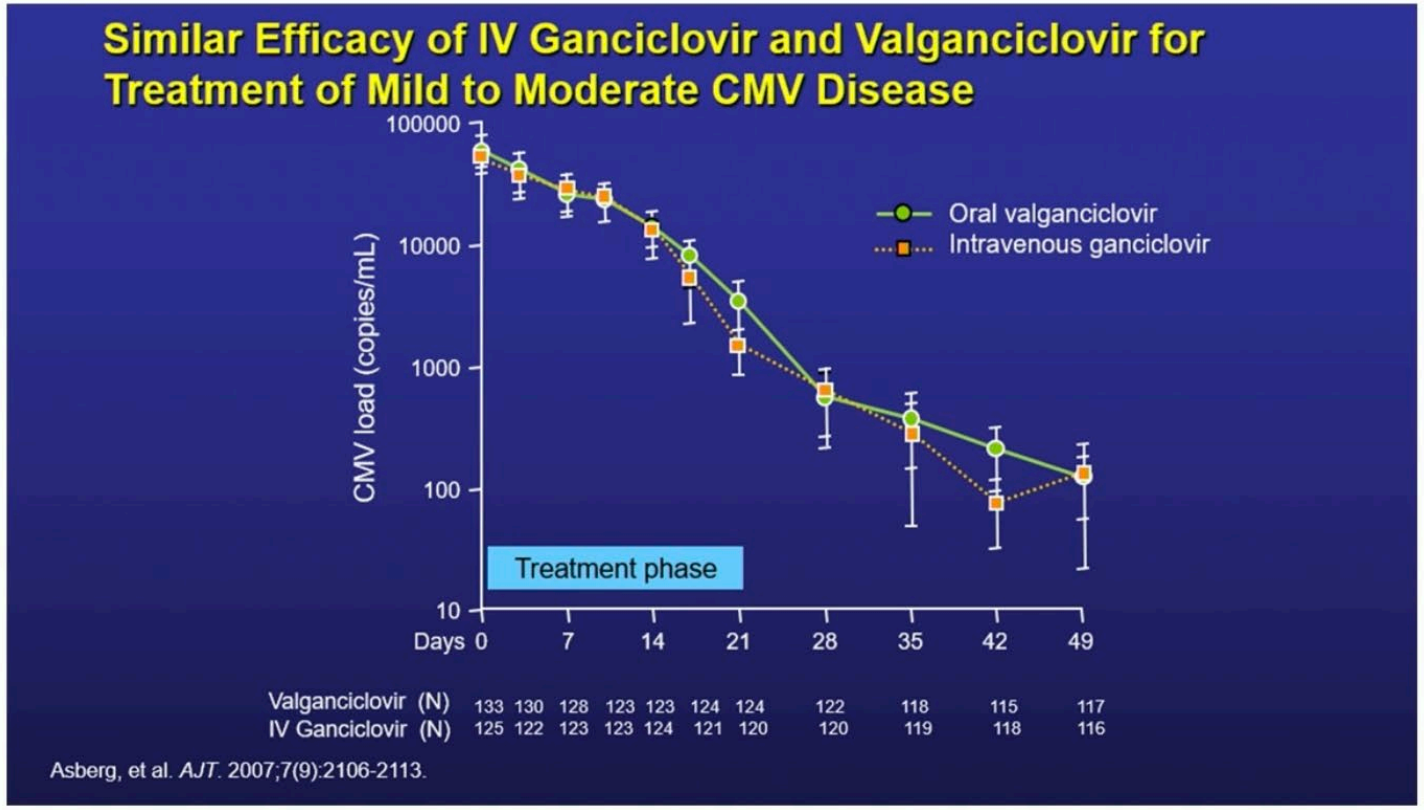
Medication*	
Oral VGCV	900 mg q12h
IV GCV	5 mg/kg q12h

Consider IV GCV initial therapy:

- Life-threatening CMV disease
- Very high viral load (assay-dependent)
- Questionable GI absorption

Not Recommended for Initial Treatment

- **Foscarnet, Maribavir, Cidofovir**
- Letermovir (not approved for treatment)



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Back to the case..

- 8 months after transplant: post-prophylaxis delayed-onset CMV with probable GI disease; CMV 975,000 |U/ml plasma
- Treated with IV ganciclovir
- Immunosuppression maintained; concerns for rejection

- 2 weeks later: clinical improvement in diarrhea, CMV PCR 310,000 IU/ml, transitioned to oral valganciclovir 900 mg PO BID

- 4 weeks later: CMV PCR 200,000 IU/ml plasma
- Bowel movement not yet back to baseline

Refractory vs Resistant CMV

Refractory CMV

- Increasing or persistent viral load (failure to decline by 1 log)

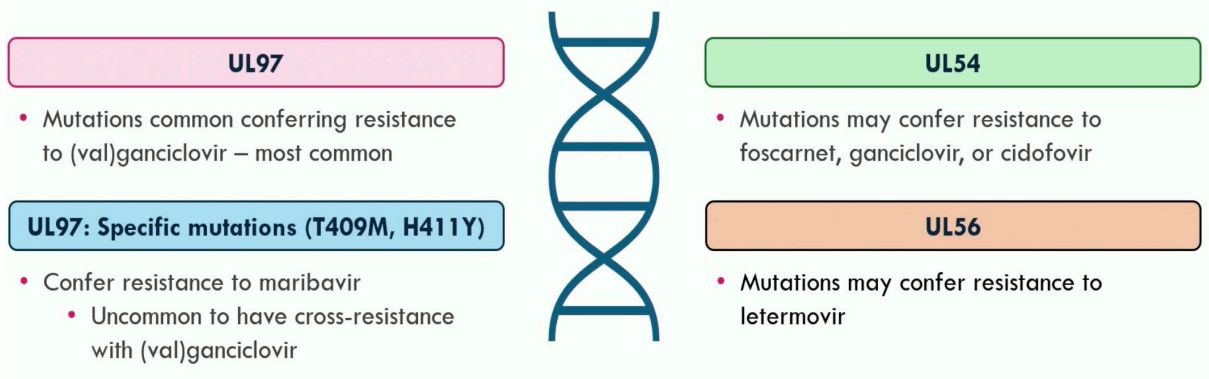
or

- Worsening or failure to improve signs and symptoms after at least 2 wks of adequate antiviral therapy

- Patients can have refractory CMV without detectable resistance

Resistant CMV

- Viral gene alteration that decreases susceptibility to 1 or more drugs (most often UL97 mutation conferring resistance to GCV)



Managing Refractory CMV: Role for Maribavir

- First step: Reduce immunosuppression; switch to sirolimus (associated with lower incidence of CMV)
- Switch anti-viral agent – Maribavir (first line), Foscarnet, high dose GCV, cidofovir (third line)
- Note, Maribavir resistance during 8 weeks of treatment reported in ~9%. NO CNS penetration.
- If concern for CNS involvement / CMV retinitis: Use Foscarnet
- Other options: IVIG, CMV-Ig

CMV Prophylaxis: Letermovir

- Inhibits CMV terminase complex (UL56→UL51/UL89)

- **Indications**

✓Primary prophylaxis: CMV-seropositive allogeneic HCT recipients

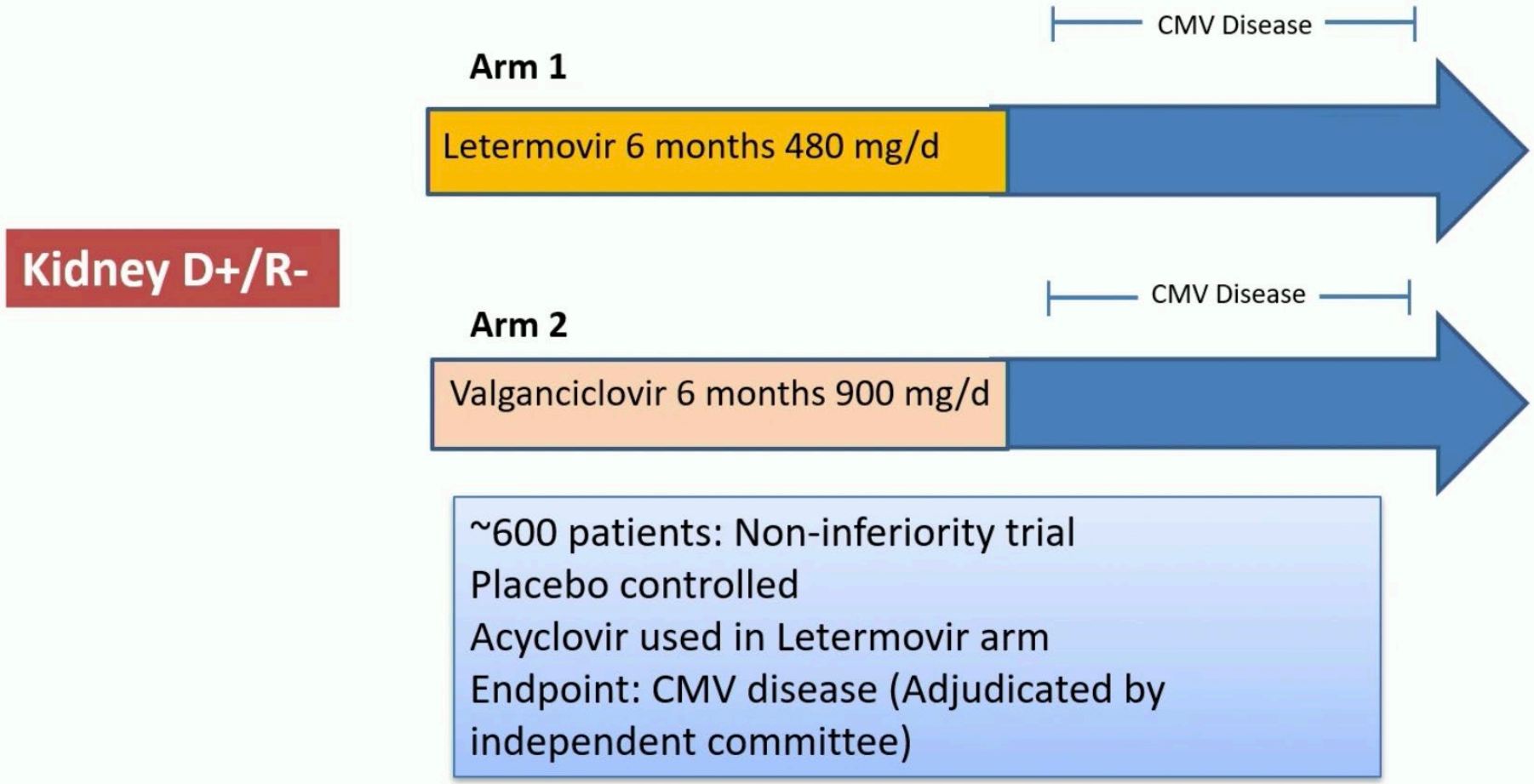
✓Prophylaxis in CMV D+/R− kidney transplant recipients

✓Off-label: SOT secondary prophylaxis, intolerance to ganciclovir, resistant CMV

JAMA | Original Investigation

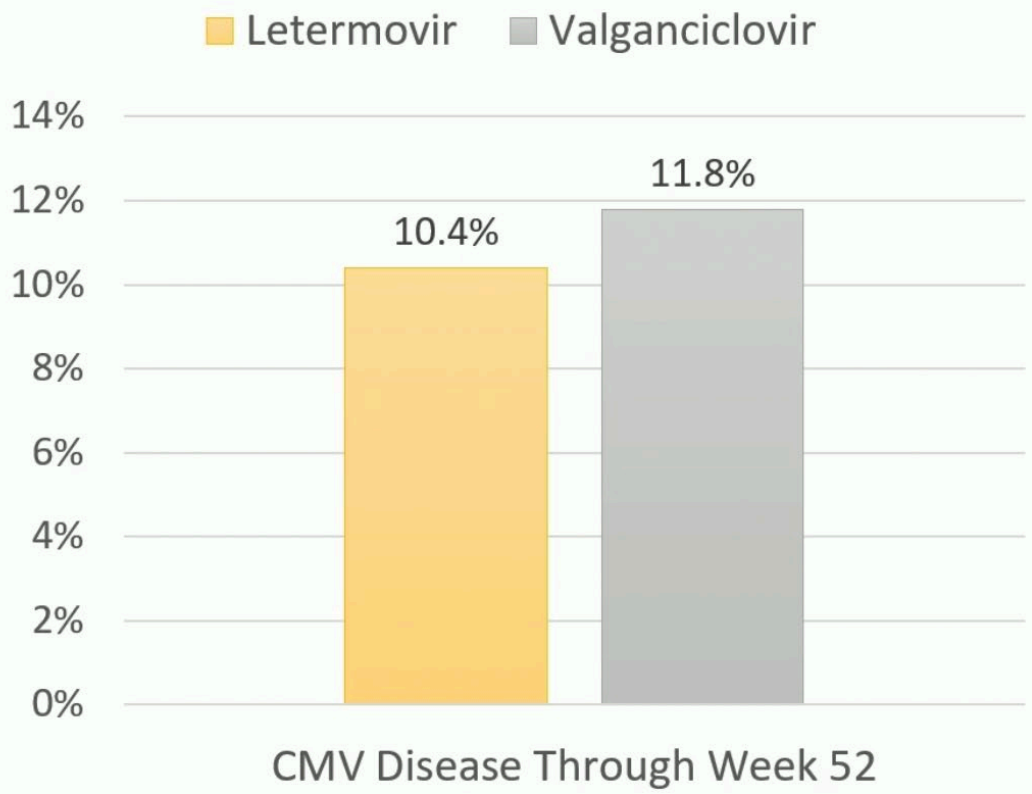
Letermovir vs Valganciclovir for Prophylaxis of Cytomegalovirus in High-Risk Kidney Transplant Recipients
A Randomized Clinical Trial

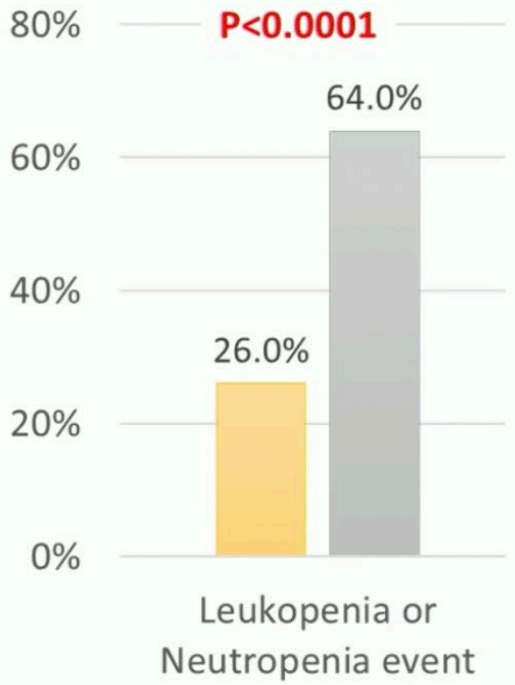
Ajit P. Limaye, MD; Klemens Budde, MD; Atul Humar, MD, MSc; Flavio Vincenti, MD; Dirk R. J. Kuypers, MD, PhD; Robert P. Carroll, BM, BCh, DM; Nicole Stauffer, BS; Yoshihiko Murata, MD, PhD; Julie M. Strizki, PhD; Valerie L. Teal, MS; Christopher L. Gilbert, BS; Barbara A. Haber, MD



~600 patients: Non-inferiority trial
Placebo controlled
Acyclovir used in Letermovir arm
Endpoint: CMV disease (Adjudicated by independent committee)

Primary Efficacy Analysis – CMV disease at 1yr





4th International Guidelines D+/R- Prophylaxis Recommendations

- For D+/R- kidney transplant recipients we recommend the use of either prophylaxis (6 months) or preemptive therapy
  - Either valganciclovir or letermovir can be used for primary prophylaxis in D+/R- kidney transplant recipients

- For D+/R- liver transplant recipients, we recommend the use of either prophylaxis (3-6 months valganciclovir) or pre-emptive therapy (PET)

- For D+/R- lung or heart we recommend prophylaxis (valganciclovir) over PET (12m for lung and 3-6m for heart)

What’s new in drugs: Anti-fungal Agents

- **Olorofim**
  - First-in-class orotomide
  - Inhibits dihydroorotate dehydrogenase (pyrimidine synthesis)
  - Minimal CYP450 interaction; low DDI risk
  - Excellent Aspergillus activity including resistant isolates
- **Fosmanogepix**
  - First-in-class Gwt1 inhibitor (mannoprotein anchoring)
  - Broad activity against yeasts and molds

Future Data

Olorofim

- Phase 3 trial completed (NCT05101187)
- Resistant/refractory invasive aspergillosis
- Concerns: resistance, breakthrough disease, azole intolerance
- Active comparator: amphotericin B

Fosmanogepix

- Ongoing clinical trial: NCT 06925321
  - Open-label, randomized vs best available therapy with salvage arm
- Target pathogens:
  - Aspergillus with limited options
  - Fusarium
  - Lomentospora prolificans
  - Mucorales
  - Other drug-resistant molds

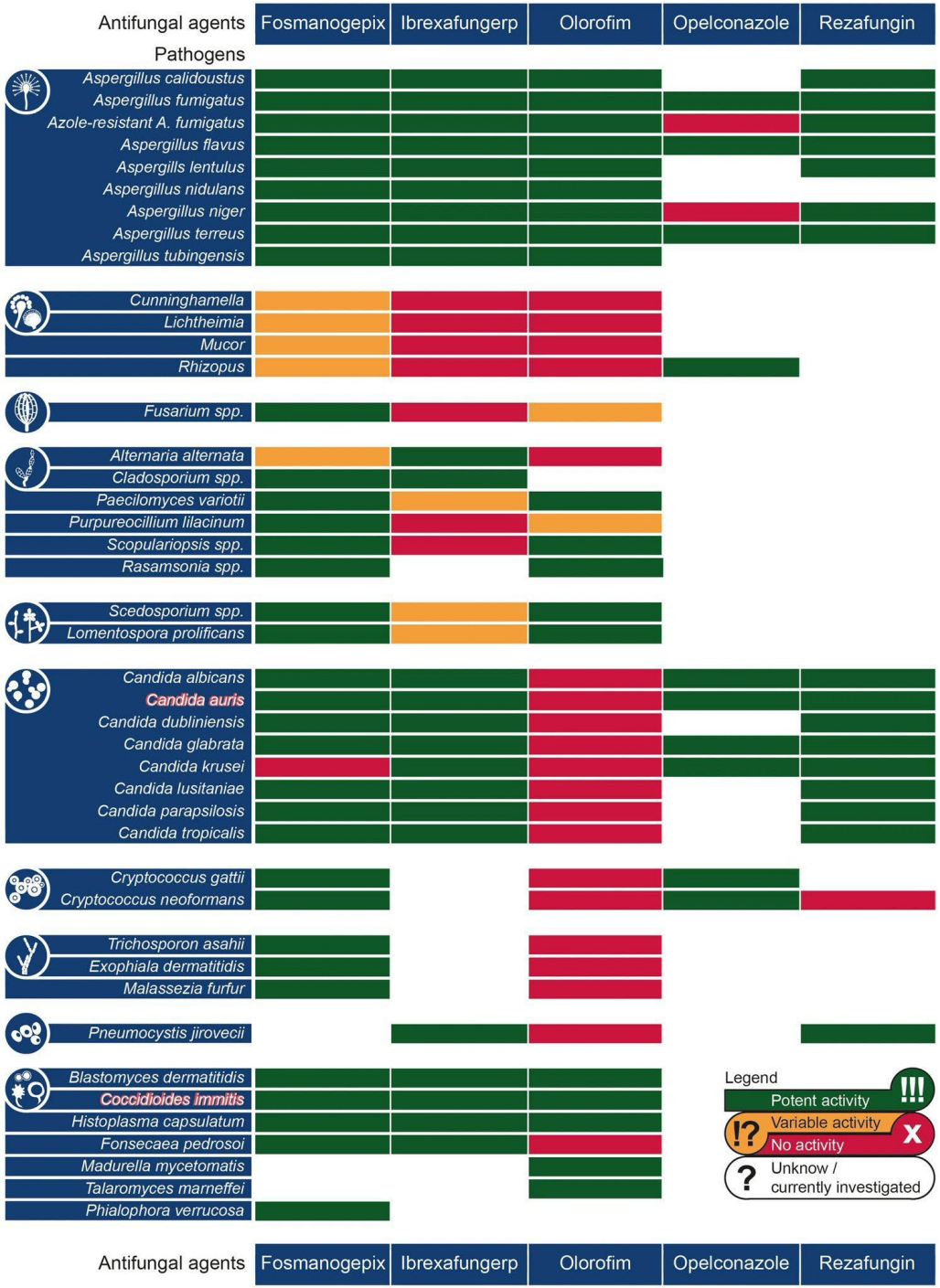
Fosmanogepix Expanded Access (Basilea)

Criteria:

- Serious and/or life-threatening
- Failed standard therapy or no available therapy
- Ineligible or no access to clinical trial
- Drug far enough along in development (actively being tested in a trial)
- Sufficient safety/efficacy data
- Sufficient evidence to expect meaningful benefit

- fosmanogepixEAP@WEPclinical.com; https://www.basilea.com/expanded-access-policy

Newer Anti-fungal agents



Hoenigl M,, et al. The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin. *Drugs*. 2021;81(15):1703-1729.

In Summary

- Bugs ≠ Drugs
- Pre-transplant Optimization and Vaccination helps prepare for transplant and decreases preventable mortality
- Maintain a low threshold to suspect & report Donor Derived Infections
- Consider Refractory CMV when there is a slow response to therapy
- There are new antibiotics and antifungals in the pipeline, use them wisely

Questions?

UM-JHS Transplant ID team

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Thank you!