Precision over Panic: A Stewardly Approach to Immunocompromised Patients with Infections

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Disclosures

- I received grant funding from Merck, Inc. and bioMeieux, Inc. for investigator-initiated projects.
- All relevant financial relationships have been mitigated.

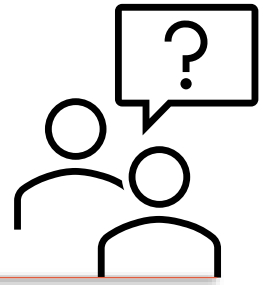
Objectives

Explain	Explain the need for antimicrobial stewardship in immunocompromised patients
Identify	Identify clinical scenarios when antimicrobial stewardship interventions can be implemented
Recognize	Recognize the infection risks associated with commonly used biologic and immunomodulatory agents

Outline

- The case for antimicrobial stewardship in immunocompromised patients
- Clinical opportunities for antimicrobial stewardship
- Infection risks associated with immunomodulatory agents

Question



Which of the following is **not** a reason for antimicrobial stewardship in immuno-compromised patients?

A. MDROs are common in hospitalized immunocompromised patients.

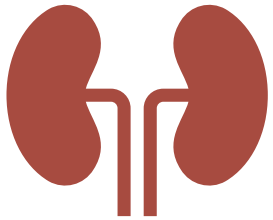
B. Antimicrobial consumption is low among immunocompromised individuals.

C. Transplant recipients require use of high-cost antimicrobials and contribute substantially to hospitals' overall antimicrobial budget.

D. Increased risk of drug toxicity due to polypharmacy and complex drug interactions occur in immunosuppressed individuals.

E. Reduced diversity of the microbiome and its' consequences.

Immunocompromised can mean many things



Impaired immune system

Cirrhosis

End stage renal disease

Diabetes mellitus

Malnutrition

Congenital immunodeficiencies

For this talk today, we'll focus on these patient groups:

Transplant recipients (solid organ or BMT)

Individuals receiving chemotherapy

Individuals receiving immunomodulatory / biologic agents

The Threat of Drug Resistance

Organ Transplants

Organ transplant recipients are more vulnerable to infections because they undergo complex surgery. Recipients also receive medicine to suppress (weaken) the immune system, increasing risk of infection.

MORE THAN 33,000 organ transplants were performed in 2016. Antibiotics help organ transplants remain possible.

Cancer Care

People receiving chemotherapy for cancer are often at risk for developing an infection during treatment. Infection can quickly become serious for these patients.

AROUND 650,000 people receive outpatient chemotherapy each year. Antibiotics are necessary to protect these patients.

CDC. Antibiotic Resistance Threats in the US, 2019

MDROs are common

Complex surgeries

Frequent and prolonged antibiotic exposures

Multiple and prolonged healthcare settings

Table 1 Summary of risk factors for infections due to MDR pathogens in SOT patients

MDR pathogen	Risk factors	Most commonly affected SOT recipients
Methicillin-resistant *S. aureus*	Colonization status, alcoholic cirrhosis, decreased prothrombin ratio, recent surgical intervention, prolonged operating time, CMV seronegative status, primary CMV infection, prior antibiotic exposure, length of hospital and ICU stay, donor derived infection	Liver, lung, heart
Vancomycin-resistant enterococci (VRE)	Colonization status, post-transplant dialysis, length of hospital stay, donor-derived infection	Liver, heart
Extended spectrum beta-lactamase producing Enterobacterales (*E. coli*, *K. pneumoniae*)	Colonization status, history of infection due to ESBL-producing organism, post-transplant treatment with corticosteroid or treatment for acute rejection, exposure to antibiotics, including 3rd generation cephalosporin, renal replacement therapy post-transplant, donor-derived infection	Liver, kidney, heart
Carbapenemase-producing Enterobacterales, mainly *K. pneumoniae* (KPC)	Colonization status, renal replacement therapy post-transplant, high model for end-stage liver disease (MELD) score at transplant, ureteral stent placement, re-transplantation, donor-derived infection	Liver, lung, kidney, kidney-pancreas
Multidrug-resistant or extremely drug resistant *P. aeruginosa*	Colonization status, cystic fibrosis, prior transplant, intensive care admission, septic shock, donor-derived infection	Lung, liver
Carbapenem-resistant *A. baumanii* (CRAB)	High pre-transplant blood urea nitrogen, hypoalbuminemia, prolonged operating time, mechanical ventilation, intensive care admission, donor-derived infection	Abdominal organs, lung

So M et al. Am J Transplant 2022;22(1):96-112.

High-Cost Inpatients

Study: Retrospective cohort, tertiary academic med center

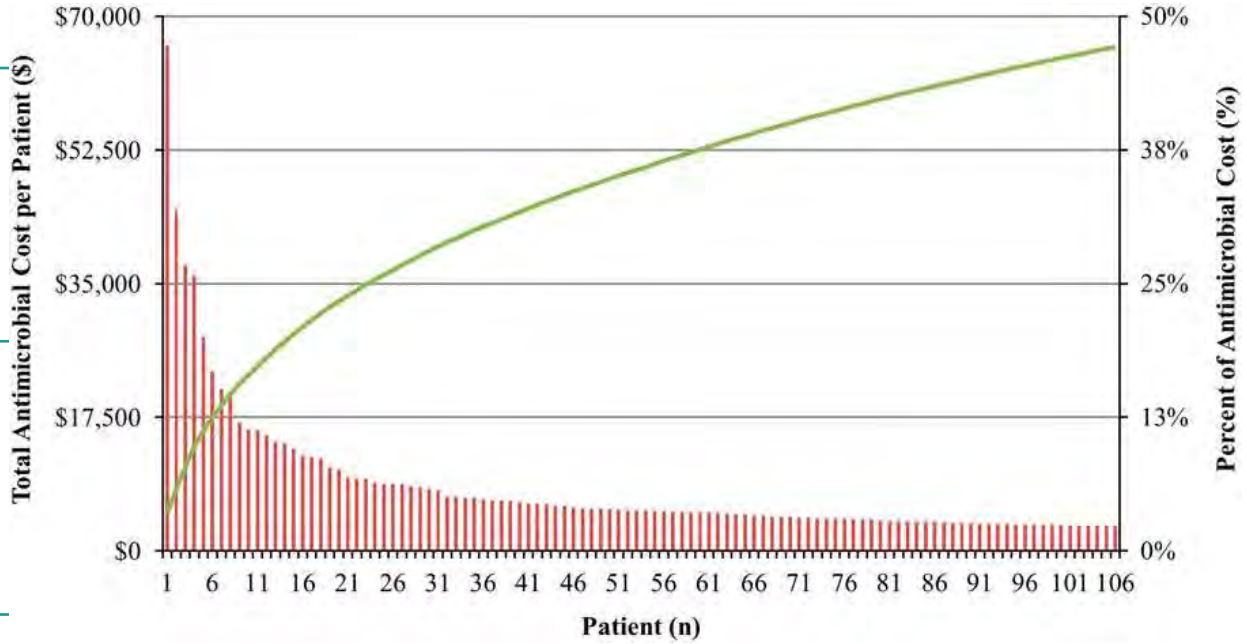
Goal: Identify top 1% patients contributing to antimicrobial budget (6 mo in 2014)

Methods: Data from pharmacy billing database.

AS program reviewed charts to determine utilization and appropriateness.

Results: From >10K patients → 106 patients (top 1%) identified as responsible for 47% of total antimicrobial budget for the study period.

47% expenditures ($890k) by 106 patients



De La Pena et al. ICHE 2017;38:259-65.

High-Cost Inpatients

TABLE 2. Demographic Characteristics of 106 Patients

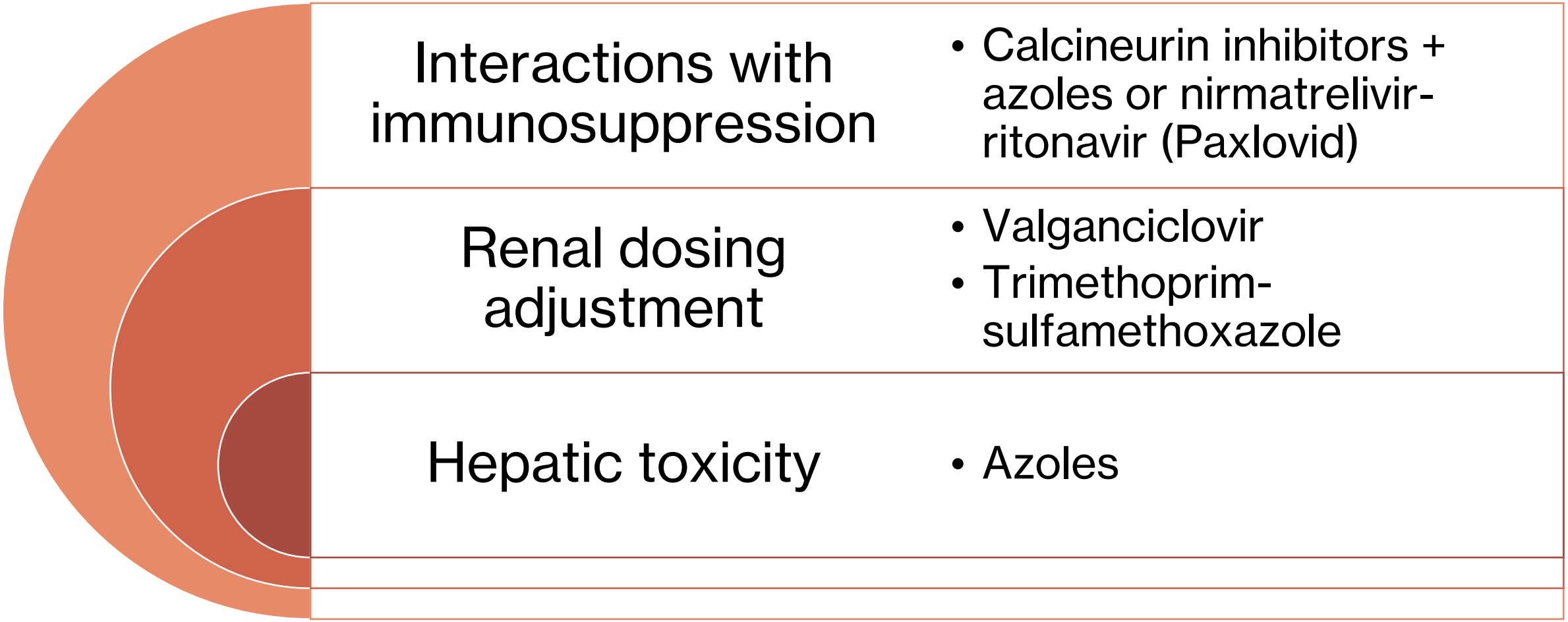
Variable	Value
Male sex, n (%)	68 (64.2)
Age, mean (SD), y	53.6 (18.7)
BMI, mean (SD)	27 (7.0)
Charlson comorbidity score, median (IQR)	6 (5–7)
Transfer from referring facility, n (%)	35 (33.0)
Inpatient ID consult, n (%)	85 (80.2)
Post-discharge ID clinic follow up, n (%)	43 (40.6)
Immunocompromised patients, n (%)	80 (75.5)
Hematologic tumor	27 (25.5)
Abdominal transplant	15 (14.2)
Diabetes mellitus	14 (13.2)
Medication-induced	12 (11.3)
Bone marrow transplant	11 (10.4)
Lung transplant	9 (8.5)
Chronic kidney disease	8 (7.5)
Cystic fibrosis	6 (5.7)
Solid oncologic tumor	4 (3.8)
HIV/AIDS	3 (2.8)
Heart transplant	1 (0.9)
Common variable immune deficiency	1 (0.9)

TABLE 3. Treatment vs Prophylaxis High-Cost Antimicrobial Regimens

Antimicrobial	Treatment	Prophylaxis	Total
Daptomycin	45	1	46
Micafungin	23	8	31
Posaconazole	8	20	28
Valganciclovir	4	13	17
Ganciclovir	8	8	16
Voriconazole	8	6	14
Liposomal amphotericin B	11	1	12
Meropenem	11	0	11
Pentamidine	0	8	8
Tobramycin (nebulized)	1	7	8
Itraconazole	0	7	7
Linezolid	7	0	7
Piperacillin/tazobactam	6	0	6
Ertapenem	6	0	6
Amphotericin B (nebulized)	0	5	5
Atovaquone	0	5	5
Rifaximin	0	5	5
Tigecycline	5	0	5
Cefepime	4	0	4
Ceftaroline	4	0	4
Foscarnet	4	0	4
Flucytosine	4	0	4

De La Pena et al. ICHE 2017;38:259-65.

Dosing & Monitoring Considerations



Emerging Transplant Infections 2021, Ch 7: 131-53.

Anti-Anaerobics in Allogeneic HCT

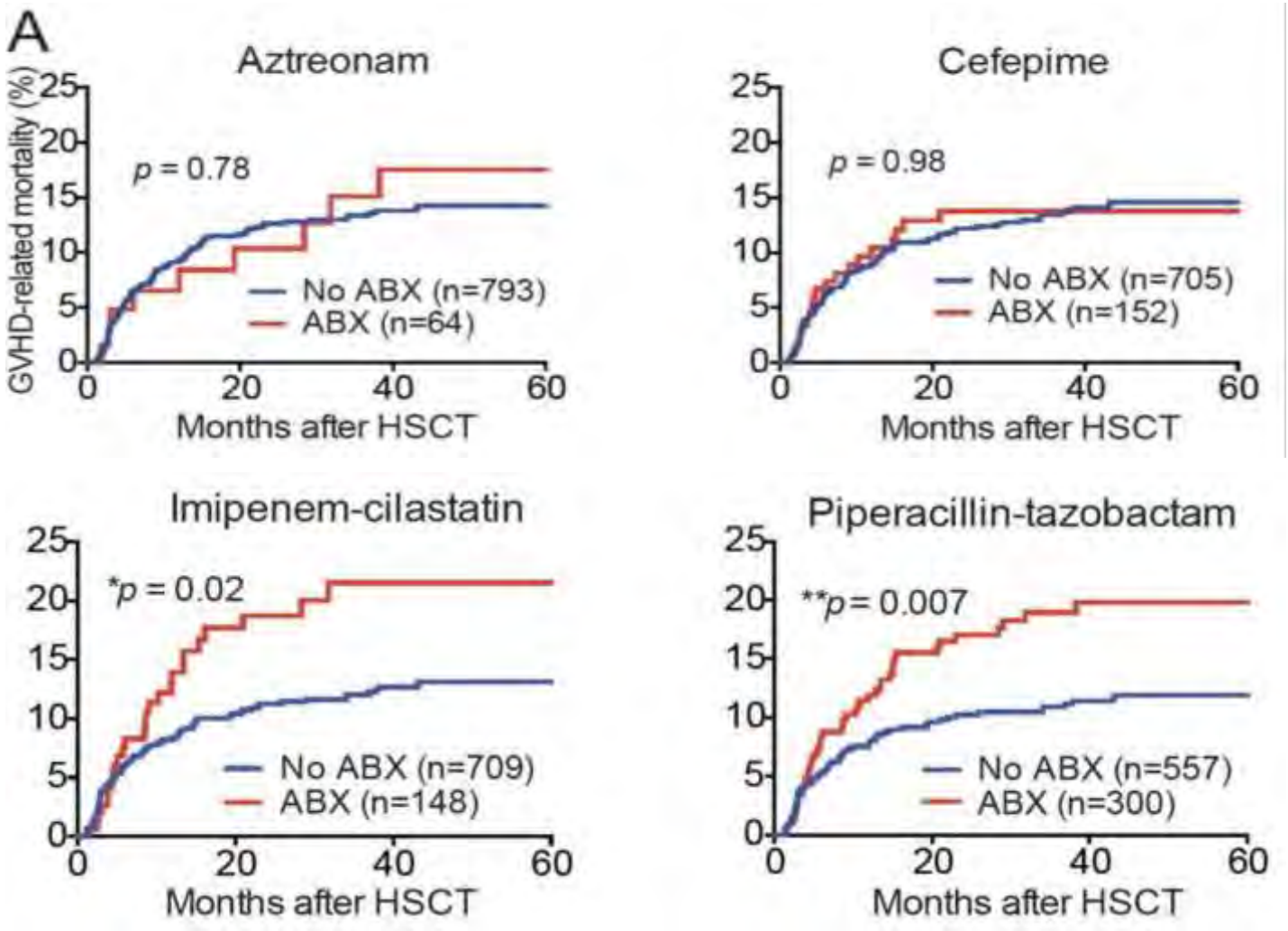
Receipt of anti-anaerobic antibiotics post-HCT

Gut Dysbiosis: reduced abundance of butyrate biosynthesis by Bifidobacteriales and Clostridiales

Acute GVHD and related mortality

Shono et al. Sci Transl Med 2016;8(339). Tanaka et al. BBMT 2020:2053-60. Elgarten et al. TCT 2021;27:177e1-8. Rashidi et al. JAMA Network Open 2023;6(6):e2317188.

GVHD-related mortality by antibiotic exposure



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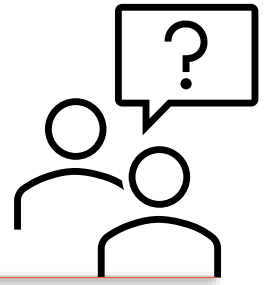

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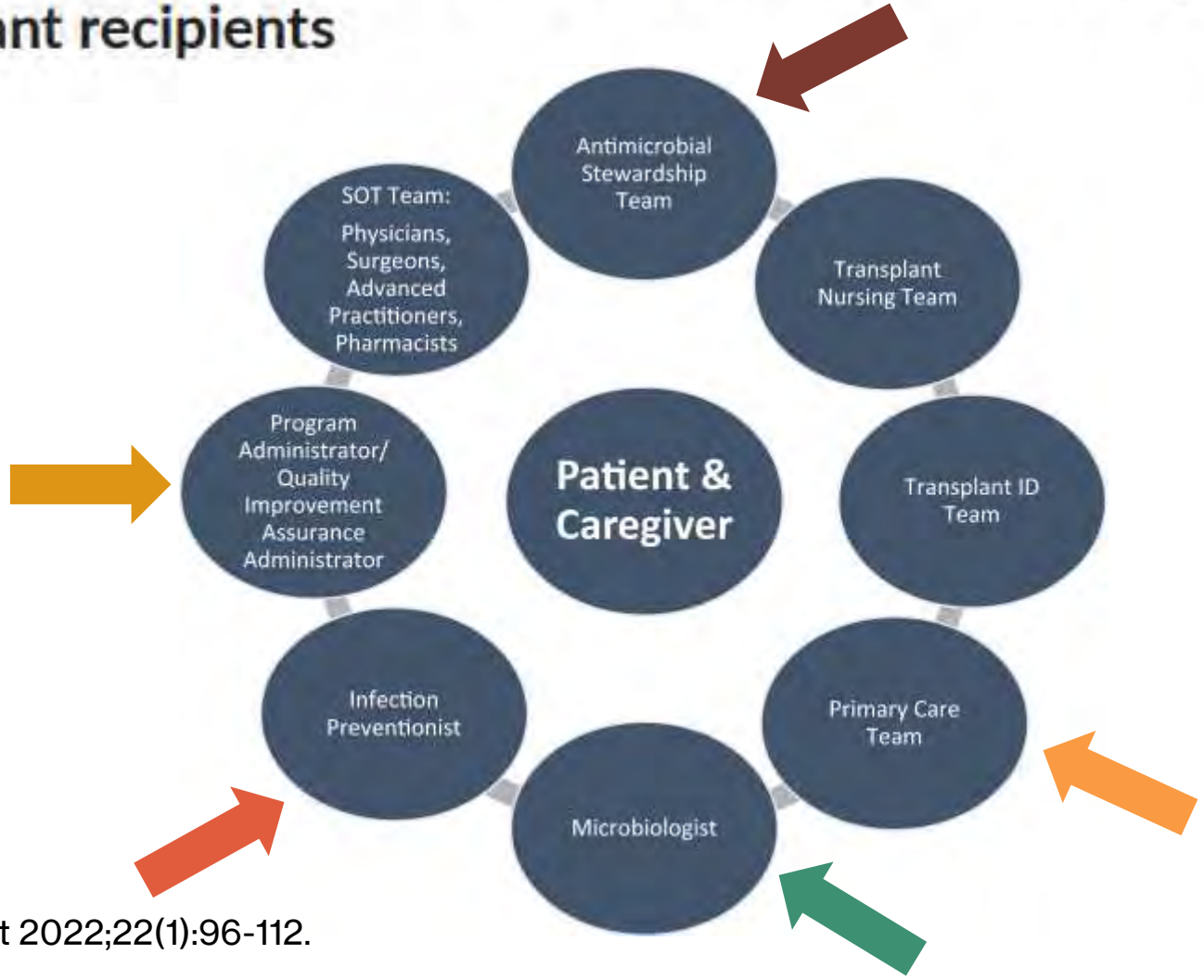
ORIGINAL ARTICLE

White paper on antimicrobial stewardship in solid organ transplant recipients



So M et al. Am J Transplant 2022;22(1):96-112.

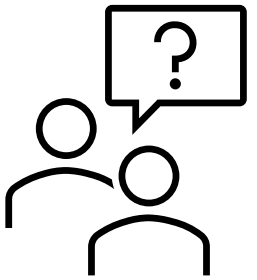
Antimicrobial stewardship challenges in immunocompromised hosts

- Provider perceptions and attitudes: “My patient is sicker than yours”
- Diagnostic uncertainty
- Impaired inflammatory responses
- Urgency for empiric effective therapy
- Significant drug toxicities and potent drug interactioins
- Prolonged exposure to prophylactic antibiotics → resistance
- Difficulty with controlling the source of infection, i.e. thrombocytopenia limiting surgical interventions
- Uncommon presentations of common and uncommon infections
- Duration of therapy not clearly defined in many infections for these patients

Abbo LM & Ariza-Heredia EJ. IDCNA 2014;28(2):263-79.

Antimicrobial Stewardship Opportunities in Immunocompromised Patients

Question



All of the following scenarios are stewardship opportunities **except**

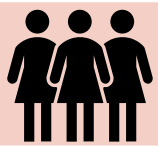
A. Avoid screening for and treating bacteriuria in renal transplant recipients

B. Early de-escalation of broad-spectrum antibiotics for febrile neutropenia in patients with high-risk hematologic malignancies.

C. Penicillin allergy evaluation and de-labeling for transplant candidates.

D. Discontinuation of acyclovir in allogeneic hematopoietic cell transplant recipients who receive letermovir prophylaxis.

Early De-escalation of Broad-Spectrum Antibiotics in Febrile Neutropenia



Population: High-risk hematologic malignancy

- MASCC score <21

Fever: fever >38.3 C or >38.0 C sustained

Neutropenia: absolute neutrophils <500 or expected to drop

Fluoroquinolone prophylaxis is common in US, less so elsewhere

Old paradigm: Upon FN, transition to broad-spectrum anti-Pseudomonal beta-lactam until neutrophil count has recovered

Freifeld et al. CID 2011;52(4):e56-93.

Early De-escalation of Broad-Spectrum Antibiotics in Febrile Neutropenia

- Early De-escalation: changing from broad-spectrum intravenous therapy to either prophylactic levofloxacin or cessation of antibiotics prior to ANC recovery

ECIL-4 (2013)	ESMO (2016)	NCCN (2022)
• De-escalate empiric antibiotics in patients (without neutropenic prophylaxis) who are clinically stable for at least **72-96 hours** and **afebrile for at least 48 hours** regardless of ANC	• Persistently neutropenic patients should be **afebrile for 5-7 days** with **no complications**, and in "certain" high-risk patients with acute leukemia, empiric therapy may continue up to 10 days	• Discontinue empiric therapy when a clinically stable patient becomes afebrile (**no minimum duration is specified**) with return to neutropenic prophylaxis, or continue until neutropenia resolves
Averbuch D. Haematologica 2013;98(12):1826-35.	Klastersky J. Annals of Oncology 2016;27:111-18.	Baden L. Prevention & treatment of cancer-related infxns. JNCCN 2022

De-Escalation Studies

Study	Hematologic Malignancy Treatment	De-escalation Strategy †	Design	Number of FN episodes +/- patients	Neutropenia Days (median)	Antibiotic Days Received (median) °	Other Results
Aguilar-Guisado 2017[57]	Chemotherapy, Auto & Allo HCT	ECIL-4 strategy °	RCT	I: 78 C: 79	I: 14 C: 11	EAT-free days: I: 16.1 C: 13.6 (p=0.026)	Mortality, fever of unknown origin, & days of fever not significantly different between groups.
de Jonge 2022[64]	Chemotherapy and HCT	Min. 72 h of carbapenem vs traditional	RCT	I: 144 C: 137	I: 10 C: 9	I: 3 C: 8 (p<0.001)	"Treatment failure" (I vs C): 19% vs 15% driven by fever recurrence (16% vs 13%) in ITT analysis.
Le Clech 2018[52] ±	Chemotherapy	ECIL-4 strategy ° (I) vs ≥ 5 days empiric BSA (II)	Prospective observational	I: 45 in 32 II: 37 in 30	I: 20 II: 12	I: 7 II: 5 (p=0.0002)	Mortality, ICU admission, relapsed fever within 48h were not significant between groups.
Verlinden 2022[53]	Chemotherapy and HCT	ECIL-4 strategy °	Retrospective cohort	I: 446 C: 512	I: 15 C: 15	I: 12 C: 14 (p=0.001)	Mortality (I vs C): 0.7% vs 2.7% (p=0.016). Recurrent fevers (I vs C): 41.6% vs 34.7% (p=0.009)
Paret 2022[65]	Chemotherapy	ECIL-4 strategy °	Retrospective cohort	I: 170 C: 178	I: 22.6 C: 20.6	I: 15.5 C: 19.9	Fever recurrence and bacteremia higher in intervention group.
Rearigh 2020[54]	Auto & Allo HCT	ECIL-4 strategy °	Retrospective cohort	I: 83 C: 214	I: 9 C: 8	I: 3.9 C: 4.6 (p=0.03)	Mortality, clinical decompensation, rehospitalization not significant.
Contejean 2022[55]	Chemotherapy & Auto HCT	ECIL-4 strategy °	Retrospective cohort	I: 217 in 148 C: 273 in 164	N/A	N/A	Glycopeptide decreased by 85% (p=0.03), carbapenem decreased by 72% (p=0.04).
La Martire 2018[56] ‡	Chemotherapy & Allo HCT	ECIL-4 strategy °	Retrospective cohort	I: 30 C: 8	19	Mean EAT-free days: 3.6	Decreased carbapenem use during intervention period.
Gustinetti 2018[57]	Allo HCT	<4 vs > 4 days empiric BSA	Retrospective cohort (early vs late de-escalation)	I: 26 C: 57	I: 17 C: 17	Median antibiotic days saved: meropenem 10, piperacillin-tazobactam 8, vancomycin 7	
Schauwvlieghe 2021[63]	Chemotherapy	Min. 72 h of meropenem	Retrospective cohort	I: 305 C: 270	N/A	I: 9 C: 19 (p<0.001)	No differences in composite ICU admissions, 30-day mortality.
Snyder 2017[58]	Allo HCT	Min. 5 days empiric BSA	Retrospective cohort	I: 46 C: 74	I: 18 C: 15	I: 8.3 C: 10.1 (p=0.028)	Recurrent fever within 72h of de-escalation (I vs C): 15% vs 19%, p=0.026. Mortality not significant.
Alegria 2022[59]	Chemotherapy	Min. 5 days empiric BSA	Retrospective cohort	I: 53 C: 40	N/A	I: 14 C: 25 (p<0.001)	Mortality, infection after de-escalation not significant.
Ly 2021[60]	Chemotherapy	Min. 7 days empiric BSA	Retrospective cohort (I: EAT ≤9 days vs C: >9 days)	I: 19 C: 25	I: 23 C: 25	7 more EAT-free days (p<0.001)	No difference in fever recurrence, ICU admission, CDI between groups.
Van de Wyngaert 2019[61]	Chemotherapy	Min. 7 days empiric BSA	Retrospective cohort	I: 62 C: 13	26	I: 10 C: 19 (p<0.001)	Fever recurred in 20% of early de-escalation group.
Kroll 2016[62]	Chemotherapy	Min. 2 weeks empiric BSA	Retrospective cohort	I: 26 C: 26	N/A	Means: I: 22.2 C: 23.5 (p=0.39)	No difference in fever recurrence
Fuller 2020[62]	Chemotherapy	Before vs until neutrophil recovery	Retrospective cohort	I (short): 38 C (long): 39	N/A	I: 9 C: 15 (p<0.01)	No difference in AEs, CDI, ICU transfers and in-hospital mortality.
Peteys 2019[50]	Auto and Allo HCT	Before vs until neutrophil recovery	Retrospective cohort	I: 24 C: 83	I: 15 C: 4	I: 8 C: 16 (p<0.006)	No difference in fever recurrence, antibiotic re-escalation, and CDI.

Stohs E, Abbas A, Freifeld A. TID 2024;e14236.

17 studies:

- 2 RCTs, 1 prospective observational, rest are retrospective cohort
- 7 adopted ECIL-4
- 5 de-escalated at 4-7 d
- 1 de-escalated > 2 wks

Variable outcome measures:

- Antibiotic-free days
- Mortality
- Fever recurrence
- ICU/clinical decompensation

How-Long Study (RCT)

Set-Up:

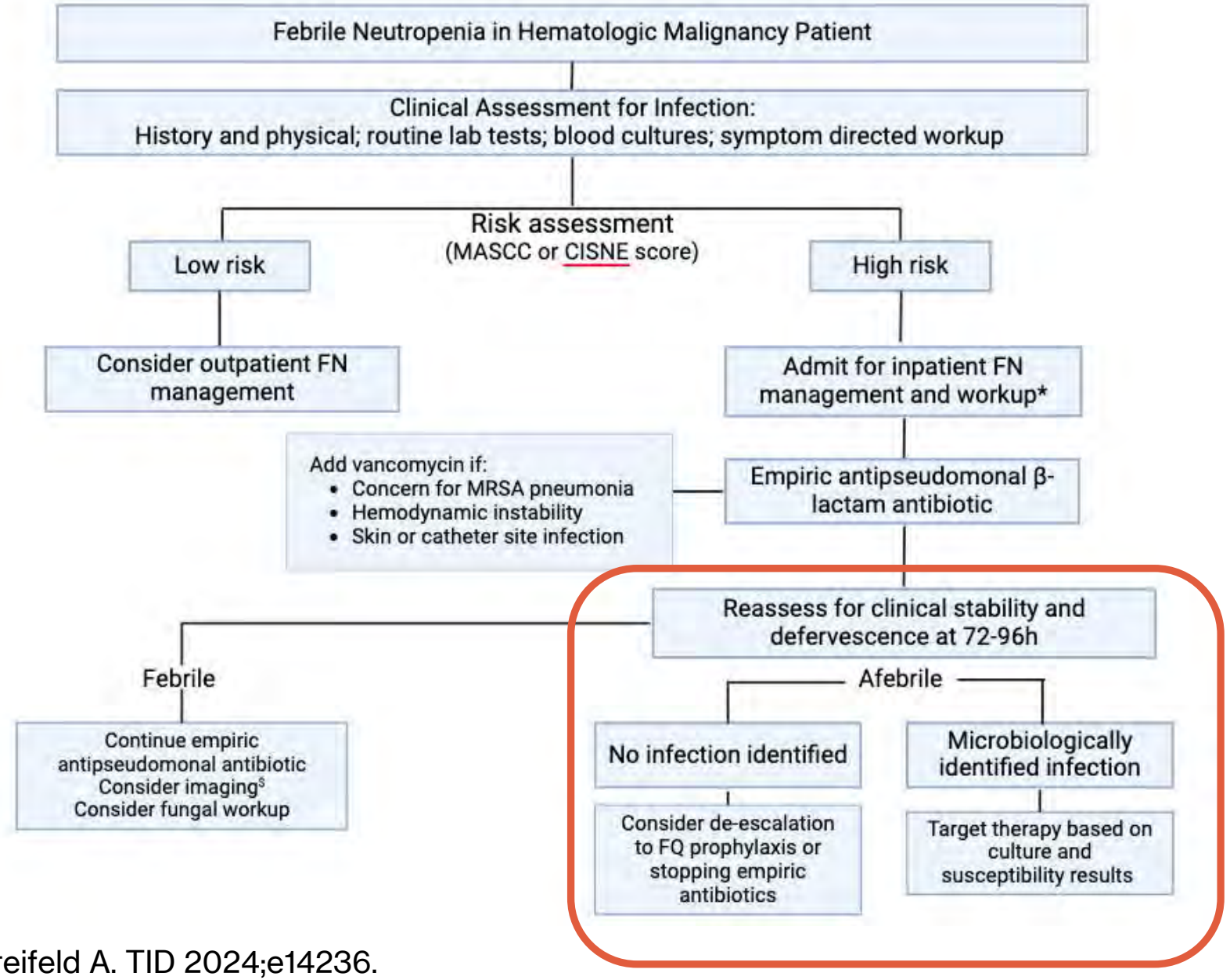
- 157 FN patients receiving chemotherapy or HCT
- De-escalation: ECIL-4 vs standard of care
- Empiric antibiotic therapy (EAT)-free days

Results:

- Shorter duration (absolute difference 6.4 days)
- No difference in
  - Crude mortality
  - Mean days of fever

Aguilar-Guisado et al. Lancet Haematol. 2017:e573-83.

A Stewardly Approach to Febrile Neutropenia



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Febrile Neutropenia - Takeaways

Empiric therapy	Target	De-escalate
• Anti-pseudomonal beta-lactam	• When microbiologic source identified	• When clinically stable and no fever x48-72h

Asymptomatic Bacteriuria in Renal Transplant Recipients

Old paradigm: Kidney transplant recipient with asymptomatic bacteriuria (ASB) should be treated

Existing guidelines

- 2019 IDSA Asymptomatic Bacteriuria Guidelines
- 2019 American Society of Transplantation ID COP - UTI in SOT

1. Don’t treat ASB if >2 mo post-transplant
2. Risk of inducing drug resistance outweighs benefit

Criticized by some, too few studies.

RCTs Comparing ASB Treatment vs No Treatment in Renal Transplant

Study	Timing of ASB	Clinical Outcomes
Coussement, CMI 2021 Multicenter RCT n = 199	≥2 months post-transplant	No difference in UTI in subsequent 12 months. Antibiotic use 5x higher in treated group. Resistant organisms emerged in treated group.
Origüen, AJT 2016 Single center RCT n = 112	≥2 months post-transplant	No difference in acute graft pyelonephritis during 2-year follow-up (primary outcome). No differences in UTI incidence, graft function or rejection, all-cause mortality, C diff infection.
Sabé, CMI 2021 Multicenter RCT n = 87	≥1 month post-transplant	No difference in acute graft pyelonephritis during 12-month follow-up (primary outcome). No difference in graft rejection or dysfunction, hospitalization, or mortality. Antibiotic resistance developed more commonly in treated group than non-treated group.
Antonio, TID 2022 Single center RCT n = 80	≤2 months post-transplant	No difference in UTI and pyelonephritis during follow-up (up to 2 months post-transplant) **Trend toward more recurrent UTIs in treated group.** **More hospitalizations in the treated group** but no difference in UTI-related hospitalizations. High baseline ESBL E. coli/Klebsiella sp but insufficient data regarding the emergence of resistance.

Table adapted from Stohs EJ & Gorlsine CA. IDCNA 2023;37(3):539-60.

Asymptomatic Bacteriuria in Renal Transplant Recipients - Takeaways

Don't screen	Don’t culture	Don't treat	Do
• Don't screen kidney transplant recipients for ASB	• Don't auto-culture UAs just because of kidney transplant	• Don't treat ASB just because kidney transplant	• Teach patients about UTI symptoms, understanding uniqueness in kidney transplant

Antibiotic Allergy De-Labeling

↑ use of narrow spectrum agents

↑ prescribing with guideline-preferred regimen

↓ Length of hospital stay

Beta-lactam Allergy

Surgical prophylaxis

Post-transplant antibiotics

Sulfamethoxazole-trimethoprim Allergy

Prophylaxis for PJP

More costly alternatives

16-17% of transplant recipients report an antibiotic allergy*

* Khumra S et al. AAC 2017;61(5). Imlay H et al. CID 2020;71(7):1587-94. Mowrer et al. TID 2022;24(5).

Antibiotic Allergy De-Labeling

De-labeling: removing allergy from chart by testing or by history taking or med reconciliation

↑ use of narrow spectrum agents

↑ prescribing with guideline-preferred regimen

↓ Length of hospital stay

Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy

The PALACE Randomized Clinical Trial

Objective

- Is oral penicillin challenge non-inferior to standard of care (penicillin skin testing followed by oral challenge) in patients with low-risk penicillin allergy?

Design

- Open-label, multicenter randomized clinical trial
- Non-inferiority margin: 5%

Setting

- Outpatient clinics in 6 medical centers in North America and Australia
- June 2018 – December 2022

Copaescu AM et al. JAMA Int Med 2023;183(9):944-52.

PEN-FAST

Externally validated tool, including immuno-compromised hosts

Trubiano JA et al. JAMA Int Med 2020;180(5):745-52.

	PEN	*Penicillin allergy reported by patient*	☐ *If yes, proceed with assessment*
	F	*Five years or less since reaction*[a]	☐ **2 points**
⊘	A	*Anaphylaxis or angioedema*	
		OR	☐ **2 points**
⊘	S	*Severe cutaneous adverse reaction*[b]	
	T	*Treatment required for reaction*[a]	☐ **1 point**
			☐ **Total points**

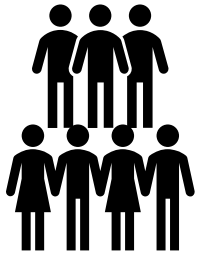
Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy

The PALACE Randomized Clinical Trial

382 Adults



20% IC

Randomization

190

Skin testing → Oral challenge

(Control)

Direct oral penicillin challenge

(Intervention)

187

Primary Outcome: Positive penicillin oral challenge

- ✓ Physician verified immune-mediated reaction
- ✓ <1 hour

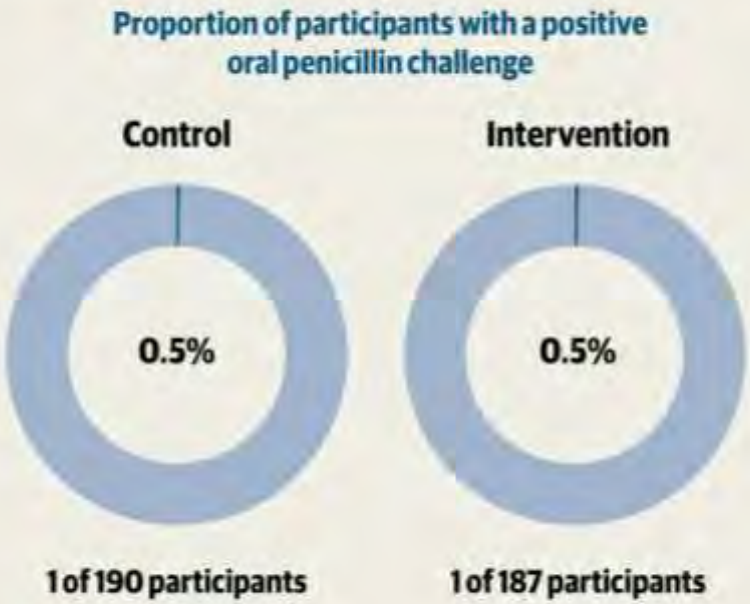
Copaescu AM et al. JAMA Int Med 2023;183(9):944-52.

Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy

The PALACE Randomized Clinical Trial

FINDINGS

The intervention was found to be noninferior to the control for the primary outcome in adults with low-risk penicillin allergy



Risk difference, 0.0084 (90% CI, −1.22 to 1.24) percentage points, which is less than the noninferiority margin

Other Findings:

- No difference in delayed immune reactions up to 5 days
- Penicillin allergy was removed in 186/190 of the control and 186/187 of the intervention group.
- 94% of participants had a PEN-FAST score <2.

Take-Aways:

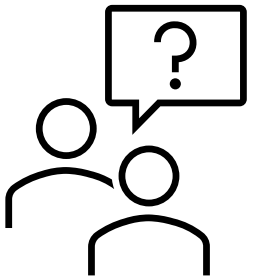
- For patients with PEN-FAST score of 0-1 → Direct oral challenge
- Shorter time in clinic
- Less expensive
- Less labor-intensive
- Adaptable to inpatient and outpatient

Copaescu AM et al. JAMA Int Med 2023;183(9):944-52.

Antibiotic Allergy- Takeaways

De-label	Optimize	Oral Challenge
• Address antibiotic allergies before transplant	• SSI prophylaxis	• Penicillin using PEN-FAST tool

Question



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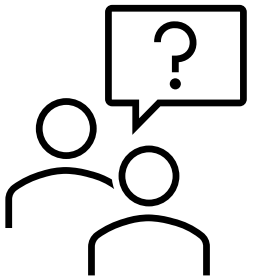
Infections in Patients on Immunomodulatory (Biologic) Agents

Question



Which of the following infections is most commonly associated with tumor necrosis factor (TNF) alpha inhibitors such as infliximab?

A. Pneumocystis pneumonia (PCP)

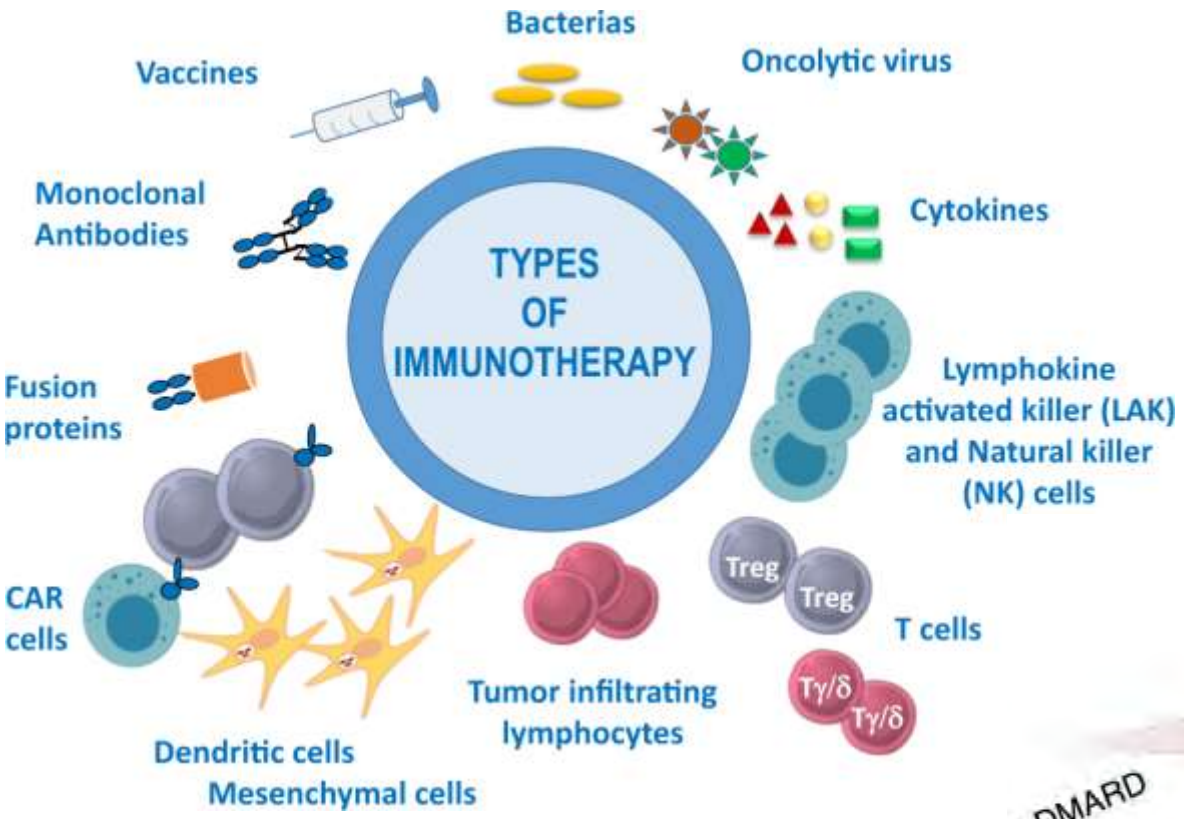
B. Reactivation of latent tuberculosis.

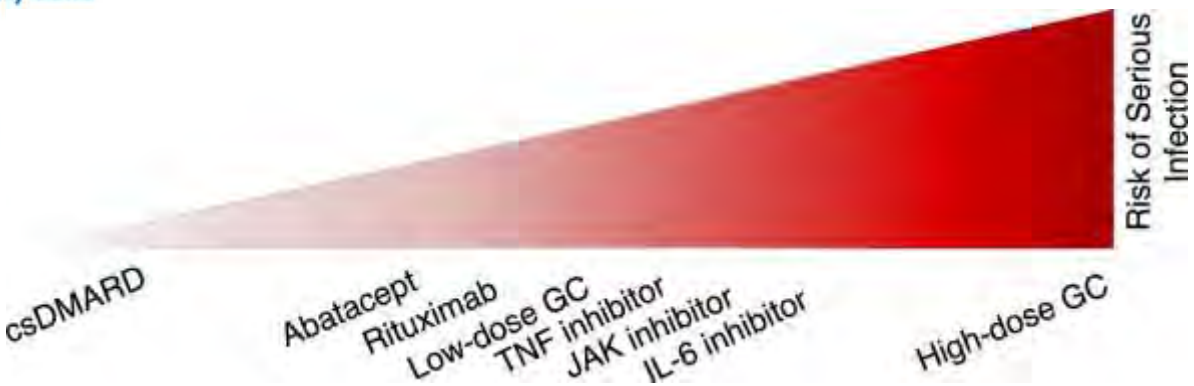
C. Herpes zoster reactivation

D. Strongyloides hyperinfection

E. Progressive multifocal leukoencephalopathy (PML)

Targeted Immunosuppression, Not One Size Fits All





Varade et al. Cellular & molecular immunology 2020;18:805-28. Riley & George. RMD Open 2021;7:e001235.

Infectious considerations and recommended screening for biologic agents

Biologic class	Examples	FDA-approved indications	Unique infectious considerations
TNF-α inhibitors	Infliximab (Remicade) Adalimumab (Humira)	RA, Crohns, psoriasis/PsA, ankylosing spondylitis, hidradenitis suppurativa	TB reactivation, histoplasmosis / endemic molds, listeriosis
Anti-CD20 (B-cell depletion)	Rituximab (Rutuxan) Obinutuzumab (Gazyva)	Non-Hodgkin lymphoma, CLL, RA, Wegener's	HBV reactivation, PCP, encapsulated bacteria, PML
IL-6/IL-1 inhibitors	Tocilizumab, anakinra	RA, giant cell arteritis, SLE, cytokine release syndrome	Intracellular bacteria, delayed CRP rise
JAK inhibitors	Tofacitinib Baricitinib	RA, alopecia areata COVID-19	TB, VZV (shingles), CMV, fungal
S1P modulators	Fingolimod (Gilenya)	Multiple sclerosis (MS)	HSV, VZV, meningitis
α1-integrin inhibitor	Natalizumab (Tysabri)	MS, Crohns	PML
Prolonged corticosteroids (1 mg/kg >2 weeks-months) often in combo therapy	Prednisone/methylpred. Dexamethasone	Too many to list	Pneumocystis, endemic mycoses (prolonged use); blunted response

Cannon et al. Ann Allergy, Asthma, Immunology 2023;130(6):718-26. Tomblyn et al. BBMT 2009;15(10):1143-1238. Furer et al. Ann Rheum Dis 2020;79:39-52.

Prevention: stewardship at the front door

Screen before initiation

- TB
- HIV, HBV
- +/- Strongyloides

Vaccinate early

- Pneumococcal, influenza, COVID-19, zoster, HBV
- Need >2 weeks to develop response

When in doubt, look at package insert

Prophylaxis

- Pneumocystis if combining biologics or with high-dose steroids
- Acyclovir / valacyclovir if at risk for HSV/VZV reactivation

Live vaccines are contraindicated once immunosuppressed (i.e. MMR)

Precision Beats Panic

Recognize atypical presentations

- Fever absent
- Low CRP/ESR
- Broader differential (fungal, viral, TB)
- CT imaging my unmask infections sooner

Treat judiciously, not generically

- Avoid reflexive vancomycin + meropenem
- Balance empiric therapy with AEs (C diff, resistance)
- Consult ID early

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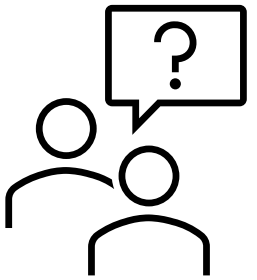

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