

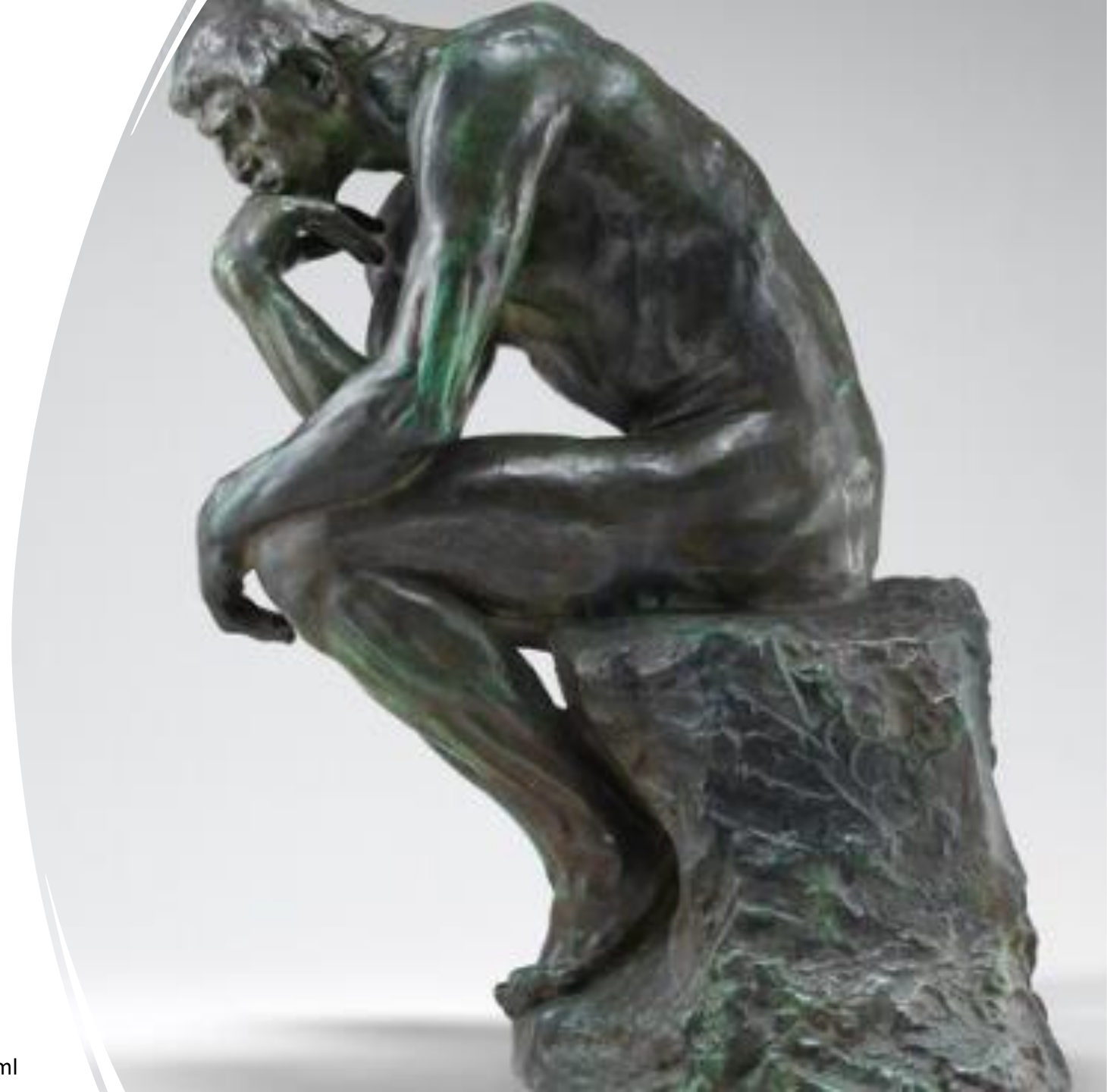
FLASCO Rapid Integration

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FLASCO Rapid Integrations

- Audience: educational initiative for clinicians new to the area of hematology/oncology
- Topic: Infectious Disease for the Hem/Onc Practitioner
- Time: 2:45-3:30 pm



Learning Objectives

- Identify up and coming anti-infective options for oncologic patients
- Recognize techniques on how to risk stratify infections in patients with cancer

NCCN Recommendations for Antimicrobial Prophylaxis

Overall Infection Risk In Patients with Cancer	Syndrome / Disease / Chemotherapy Examples	Antimicrobial Prophylaxis
Low	NP < 7d Majority of solid tumor chemotherapy regimens	None except if history of VZV then consider antiviral
Intermediate	7d < NP < 10d Lymphoma Multiple myeloma Purine analog therapy (fludarabine) CAR T	Bacterial: consider FQ while NP Fungal: consider antifungal while NP Viral: consider while NP and longer if needed PJP: consider depending on the Rx
High	NP > 10d Induction AML / consolidation Alemtuzumab therapy Allogeneic transplant GVHD	Bacterial: consider FQ while NP Fungal: consider antifungal while NP Viral: consider while NP and longer if needed PJP: consider depending on the Rx

NP: neutropenia, CAR T: chimeric antigen receptor therapy, AML: acute myelogenous leukemia, GVHD: graft vs host disease, VZV: varicella zoster, FQ: fluroquinolone, Rx: drug

NCCN Recommendations for Immune and Targeted Treatments

Mechanism of Action	Agents	Major Uses	Infection Concerns	Recommendations
CD 20	Obinutuzumab Ofatumumab Rituximab	CLL, FL CLL CLL, NHL, ALL	HBV (high risk) HCV HSV / VZV PML	Screen for infections at baseline. Treat as needed per international guidelines. Consider prophylaxis for HSV / VZV / PJP. Monitor for drug-induced NP / lymphocytopenia / hypogammaglobulinemia
CD 33	Gemtuzumab ozogamicin	AML	Bacterial infxn OI PJP	Monitor for drug-induced VOD / hepatotoxicity Monitor for NP enterocolitis and interstitial pneumonitis
CD 38	Daratumumab Isatuximab	MM ALL (T-cell)	<i>Listeria</i> HBV HSV / VZV CMV PJP <i>Cryptococcus</i>	Recommend HSV / VZV prophylaxis Consider PJP prophylaxis Monitor for drug-induced NP

HBV: hepatitis B virus, HCV: hepatitis C virus, HSV: herpes simplex virus, VZV: varicella zoster, PML: progressive multifocal leukoencephalopathy, infxn: infection, OI: opportunistic infection, PJP: Pneumocystis, VOD: veno-occlusive disease

AML Case

Work Up

- EKG
- 2D Echo
- Weight
- CT sinus without contrast
- CT chest without contrast
- Any special medical history

Prophylaxis

- Fluroquinolone > Cefdinir
- Micafungin then Triazole
- Acyclovir

AML Case

Neutropenic fever

- Persistent temperature of 100.4°F > 1 hr
- Or
- Single temperature of 101°F

Pan culture

- All lumens that are accessed + peripheral blood culture
- Urinalysis +/- urine culture (if with symptoms)
- Lactic acid
 - NP fever can present with or without sepsis
- Respiratory PCR panel
- Radiology

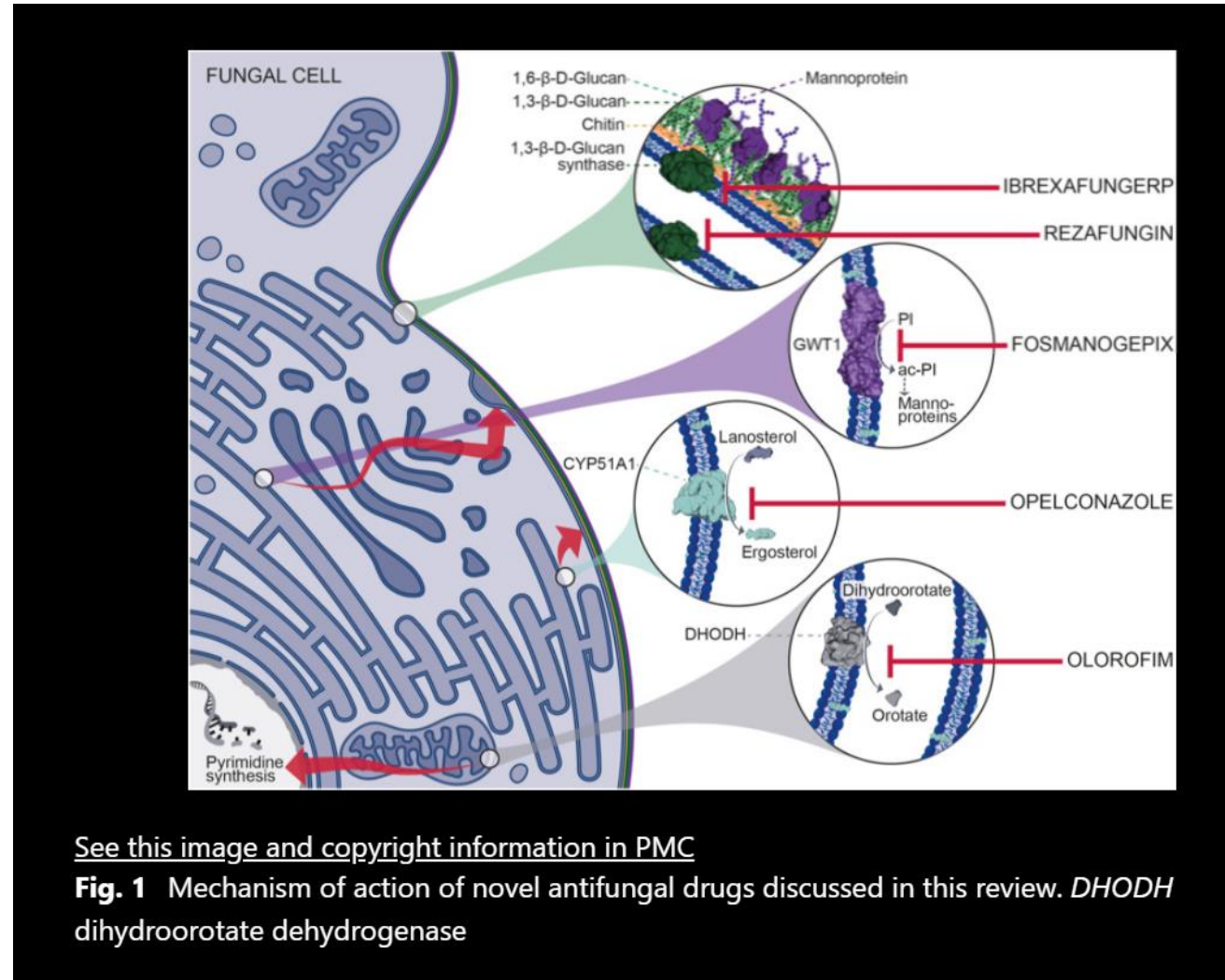
AML Case

	Gram Negative Coverage (esp anti-Pseudomonas)	<i>Enterococcus</i> Coverage	Gram Positive Coverage	Anaerobic Coverage	Extended Spectrum Beta Lactamase Producing (ESBL) Coverage
Cefepime	+		+		
Pip-tazo	+	++	+	+	
Meropenem	+	+	+	+	+

Allogeneic Transplant Patients and CMV Prophylaxis

- Letermovir
 - Inhibitor of CMV terminase complex
 - No activity on other herpes viruses (so the pt also needs to take acyclovir)
 - NOT approved for treatment of CMV
 - Can be taken by mouth or by IV
- Letermovir prophylaxis for CMV in HSCT (Marty et al, NEJM 2017)
 - From approx. day 5 to day 100
 - Phase 3, double blind trial for CMV seropositive recipients
 - Results: lower rates of clinically significant CMV infection over placebo
- Among the transplant programs in the US, this is now the standard of care.

Antifungal Pipeline



Antifungal Pipeline

Drug	Against What	Special
Fosmanogepix	Invasive candidiasis Aspergillosis Scedosporiosis Fusariosis Mucormycosis Cryptococcosis Coccidiomycosis	There might be synergy with liposomal amphotericin B
Ibrexafungerp	Invasive candidiasis INCLUDING <i>C. auris</i> and <i>C. glabrata</i> Aspergillosis	Potential for an oral step-down therapy
Olorofim	MDR molds	
Rezafungin	<i>Candida</i> sp, <i>Aspergillus</i> sp, PJP	Echinocandin with long half life (qwk)

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim ..., Hoenigl et al, Drugs 2021

Antimicrobial Stewardship in a Cancer Center

It does not increase rates of:

- Sepsis
- Death related to infections
- Resistance issues

Look for opportunities to de-escalate

- Post transplant cyclophosphamide
→ high rates of CRS
→ 24hrs later → de-escalate
- If cultures neg x 5d, pt is AF and stable → de-escalate

De-escalation is different than narrowing therapy

- Narrowing therapy is based on a positive culture with sensitivities

Diagnostics

Speak to your local lab

- How long do blood cultures get held → 5 days
- How often do CMV PCRs get done per week → 4x per week
- How often do EBV PCRs get done per week → 3x per week
- Which items gets sent out to a reference lab? Which reference lab? → ARUP

Multiplex PCRs

- BioFire® (as an example)
 - Respiratory panels
 - Blood culture panels
 - GI PCR panels
 - Meningitis encephalitis panels

MALDITOF

- They have bacterial, fungal and AFB libraries

Diagnostics

- Microbial cell free DNA (cfDNA) test for microbes
 - Karius® (currently the only example company available in the US)
 - CLIA certified for inpatient use
 - Approximately 30 hours for door-to-door turnaround time
 - Depending on the number of samples your hospital orders, the price shifts
 - Approx \$2,000 / lab at Moffitt at this juncture
 - Helps the multidisciplinary team make unusual diagnoses
 - Example
 - Pt status post alloHSCT (approx. 25d) had fevers x 7d
 - Blood cxs / ucx / imaging: negative
 - #1 Karius®: toxoplasmosis at the amount of 54,000
 - #2 Karius® (after about 4 wks of high dose TMP SMX): toxoplasmosis at the amount of 89
 - Added benefit of a quantitative amount to show improvement in the infection

Goals and Objectives

Key Topics for Heme / Onc

- NCCN Recommendations for Antimicrobial Prophylaxis
- NCCN Recommendations for Immune and Targeted Treatments
- AML Case
 - Neutropenic Prophylaxis
 - Neutropenic Fever
- Allogeneic Transplant Patients and CMV Prophylaxis
- Antifungal Pipeline

Antimicrobials Stewardship in a Cancer Center

Diagnostics

Questions?



Welcome to our multidisciplinary Antimicrobial Stewardship Team at Moffitt Cancer Center.

We are clinical infectious diseases providers, clinical infectious diseases / ASP pharmacists, microbiology, infection prevention and staff.

We meet quarterly to help Moffitt Cancer Center give the best care possible to its patients.

