MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

GUIDELINES FOR CAR-T INFECTION PROPHYLAXIS

I. PURPOSE: CAR-T patients are at risk for infections in the post-transplant period.

II. SCOPE: This guideline outlines the routine infection prophylaxis for at risk patients.

III. GUIDELINE:

PCP/PJP Prophylaxis	Antifungal Prophylaxis
Antibacterial Prophylaxis	Antiviral Prophylaxis
References	

Table 1. Prevention of PCP/PJP (Pneumocystis carinii/jirovecii) pneumonia

Population	First Choice	Alternatives
All Adult patients Start: Aerosolized **pentamidine** 300 mg between day -10 to day -1	Continue **pentamidine** until ≥day 30, ANC >1000, and PLT >50, then: **TMP-SMX** 1 DS tab PO BID, 2 days per week (i.e., M & Th) Duration of PCP prophylaxis: Stop after 3 months provided CD4 >200 cells/mm^3	**Pentamidine** 300 mg inh once monthly **Pentamidine** 4 mg/kg IV once monthly (if unable to tolerate inhaled; dosed using actual body weight) **Dapsone*** 100 mg PO daily **Atovaquone** 1500 mg PO daily w/food
All Pediatric patients Start: Aerosolized **pentamidine** 300 mg (if old enough to tolerate) -OR- IV **pentamidine** 4 mg/kg between day -10 to day -1	Continue **pentamidine** until ≥day 30, ANC >1000, and PLT >50, then: **TMP-SMX** 2.5 mg/kg TMP PO BID, 2 days per week (max = 160 mg TMP/dose) Duration of PCP prophylaxis: Stop after 3 months provided CD4 >200 cells/mm^3	**Pentamidine** 300 mg inh once monthly **Pentamidine** 4 mg/kg IV once monthly (if unable to tolerate inhaled; dosed using actual body weight) **Dapsone*** 2 mg/kg/dose PO daily (max: 100 mg) **Atovaquone (Mepron)** – w/food 1-3 months: 30 mg/kg PO daily 4-24 months: 45 mg/kg PO daily >24 months: 30 mg/kg PO daily Max: 1500 mg/dose

*Be aware of increased risk of methemoglobinemia. G6PD screening recommended for African Americans, Indians, or Mediterranean descent.

Table 2. Antifungal Prophylaxis

Population	First Choice	Alternatives
All Adult patients Start: with lymphodepleting chemo or on day 0	**Fluconazole** 200 mg IV/PO daily **Posaconazole** 300 mg PO/IV daily if one of the following: 1) Methylprednisolone (Medrol) ≥1 mg/kg for ≥7 days 2) ANC <1000 for ≥10 days 3) Additional immunosuppression (i.e., tocilizumab, ruxolitinib, etc.) Duration of antifungal prophylaxis: 1) Until ANC >1000 2) Prednisone <10 mg/day	Alternative to fluconazole: **Micafungin** 50 mg IV q24h If AST/ALT/T.Bili >3x ULN or otherwise deemed clinically significant Alternative to posaconazole: **Micafungin** 100 mg IV q24h If AST/ALT/T.Bili >3x ULN or otherwise deemed clinically significant
All Pediatric patients Start: with lymphodepleting chemo or on day 0	**Fluconazole** 3 mg/kg IV/PO daily (max: 200 mg) **Posaconazole**^ PO/IV daily if one of the following: 1) Methylprednisolone (Medrol) ≥1 mg/kg for ≥7 days 2) ANC <1000 for ≥10 days 3) Additional immunosuppression (i.e., tocilizumab, ruxolitinib, etc.) **Posaconazole** tablet dosing: <40 kg: 100 mg PO BID 40-60 kg: 200 mg PO BID >60 kg: 300 mg PO BID Duration of antifungal prophylaxis: 1) ANC >1000 1) Prednisone <0.15 mg/kg/day	Alternative to fluconazole: **Micafungin** 3-4 mg/kg IV q24h (max: 50 mg) If AST/ALT/T. bili >3x ULN or otherwise deemed clinically significant Alternative to posaconazole: **Micafungin** 5 mg/kg IV q24h (max: 100 mg) If AST/ALT/T.Bili >3x ULN or otherwise deemed clinically significant

^**Posaconazole**: trough levels are preferred with goal ≥700 ng/mL for prophylaxis and ≥1250 ng/mL for treatment.

Table 3. Antibacterial Prophylaxis		
Population	**First Choice**	**Alternatives**
All Adult patients Start: On day +1	**Levofloxacin** 500 mg PO/IV daily Duration of antibacterial prophylaxis: 1) Febrile neutropenia (i.e., broader antimicrobial such as cefepime, etc.) -OR- 2) ANC >1000 after day +10	**Cefpodoxime** 200 mg PO BID
All Pediatric patients Start: On day +1	**Levofloxacin** <5 years: 10 mg/kg/dose PO/IV BID (max: 500 mg/dose) ≥5 years: 10 mg/kg/dose PO/IV daily (max: 500 mg/dose) **Duration of antibacterial prophylaxis** 1) Febrile neutropenia (i.e., broader antimicrobial such as cefepime, etc.) -OR- 2) ANC >1000 after day +10	**Cefpodoxime** 5 mg/kg PO BID (max: 200 mg)

Table 4. Antiviral Prophylaxis

Virus	Population	First Choice	Alternatives
HSV/VZV prophylaxis	All seropositive adult patients Start: On day 0 (unless already taking)	**Acyclovir** 400 mg PO BID Duration of antiviral prophylaxis: 1 year	**Acyclovir** 2.5 mg/kg IV q12h **Valacyclovir** 500 mg PO daily **Famciclovir** 250 mg PO BID
	All seropositive pediatric patients Start: On day 0 (unless already taking)	<6 years: **Acyclovir** 200 mg PO BID ≥6 years: **Acyclovir** 400 mg PO BID Duration of antiviral prophylaxis: 1 year	**Acyclovir** 2.5 mg/kg IV q12h
Immunoglobulin Supplementation (IVIG)		Start: **IVIG** 0.4 g/kg/dose x1 as an outpatient between day -10 to -1. Frequency (monthly): Replete when IgG <300 mg/dL or 300-500 mg/dL with frequent infections	

Antiviral monitoring for CMV, EBV, HHV-6, etc. viral monitoring frequency at the discretion of the treating physician.

REFERENCES:

1. FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing and Administration, Seventh Edition 2018.
2. Hill JA, Li D, Hay KA, Green ML, Cherian S, Chen X, Riddell SR, Maloney DG, Boeckh M, Turtle CJ. Infectious complications of CD19-targeted chimeric antigen receptor-modified T cell immunotherapy. Blood. 2018 Jan 4; 131(1):121-130.
3. Maude SL, Frey N, Shaw PA, Aplenc R, Barrett DM, Bunin NJ, Chew A, Gonzalez VE, Zheng Z, Lacey SF, Mahnke YD, Melenhorst JJ, Rheingold SR, Shen A, Teachey DT, Levine BL, June CH, Porter DL, Grupp SA. Chimeric antigen receptor T cells for sustained remissions in leukemia. N Engl J Med. 2014 Oct 16;371(16):1507-17.
4. NCCN Clinical Practice Guidelines in Oncology: Prevention and Treatment of Cancer-Related Infections. J Natl Compr Canc Netw. 2016 Jul;14(7):882-912.

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