KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 37.YIL

BAŞKENT ÜNİVERSİTESİ 1993

CUMHURİYETİMİZ 100 YAŞINDA

Hematolojik Malignitelerde Profilaksi

Dr. Özlem Kurt Azap

Başkent Üniversitesi Tıp Fakültesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

Yanıt aradığımız sorular

- Hangi hastalıklar/hastalar/rejimler için profilaksi gerekiyor?

- Hangi profilaktik ilaçlar, ne kadar süre kullanılıyor?
  - Anti-bakteriyel
  - Anti-fungal
  - Anti-viral

Kaynaklar

- ECIL dökümanları
- Makaleler
- Hastanelerden örnekler

ECIL: European Conference on Infections in Leukemia

ecil-leukaemia.com/en/

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Welcome message - Committee

Dear Colleague,

On behalf of the Organization Committee we are pleased to welcome you for the ninth ECIL meeting.

In 2005, we had our first, almost experimental, meeting, initiated by the four participating bodies: the EORTC Infectious Diseases Group, the EBMT Infectious Diseases Working Party, the Supportive Care Group of the ELN, and the Immunocompromised Host Society. Fourteen years later, ECIL has matured, and has earned its place as an authority in advising how best to deal with infectious complications of immunocompromised patients. ECIL has also come of age and is now a non-for profit organization thereby securing its future and safeguarding its autonomy.

ECIL has always sought to include the widest range of specialists in infectious diseases of the immunocompromised patients be they clinicians, microbiologists, oncologists, haematologists to help define new areas of research. Since its inception, ECIL has published 34 articles in peer reviewed journals and 35 slide sets on a variety of infectious disease topics with the main ones being regularly updated. Thanks to your expertise, you all have been able to create, debate, and issue guidelines for the wider community.

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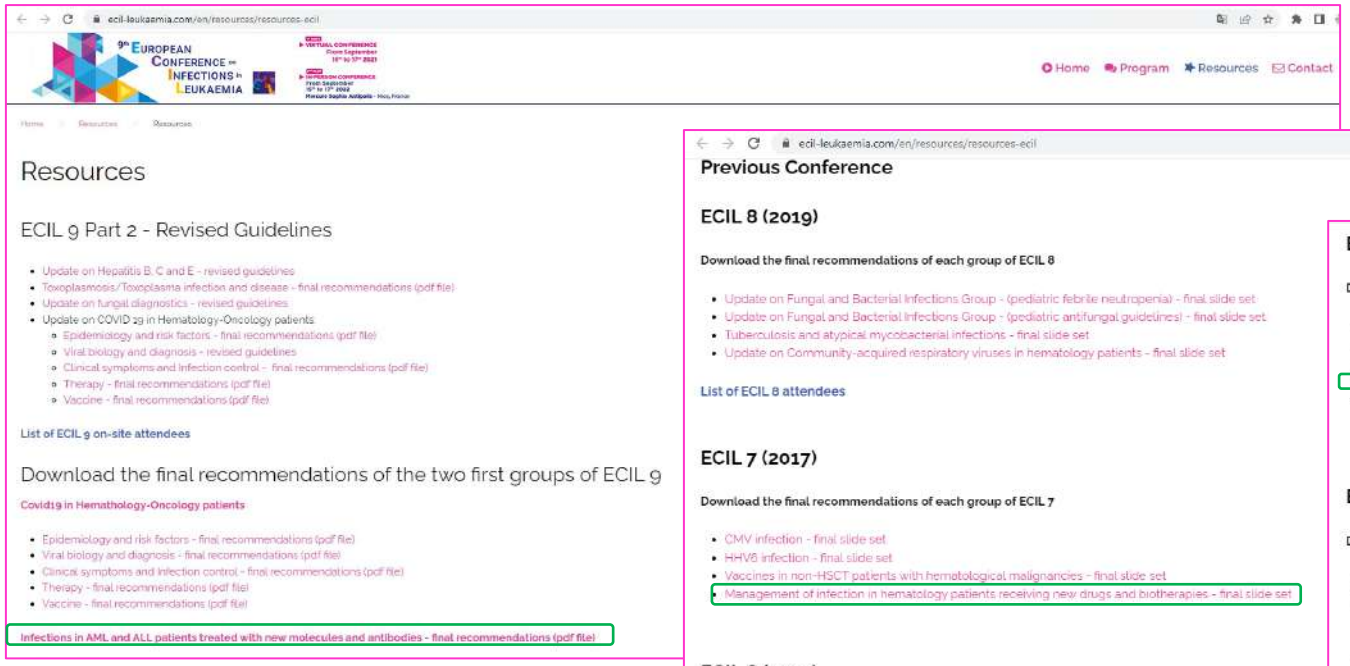
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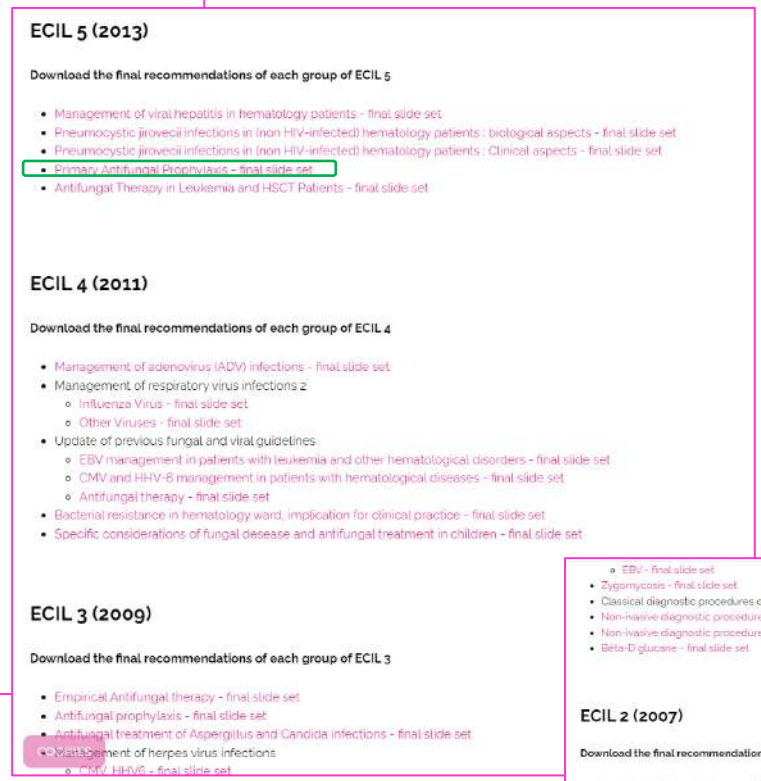
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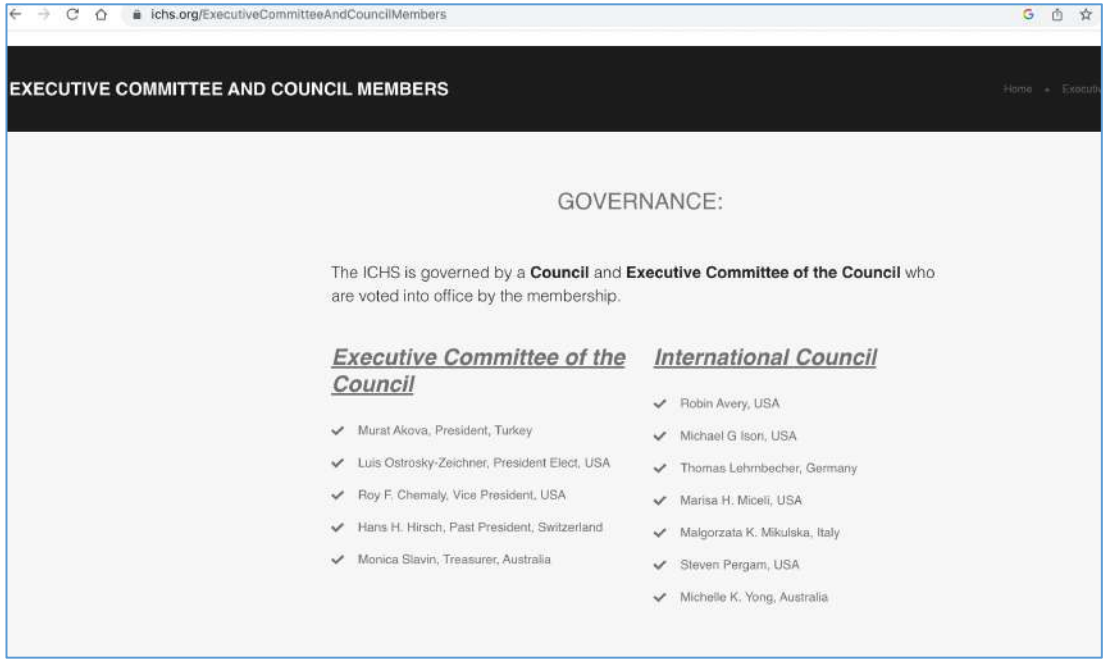

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Enjoy ECIL 9!

Best wishes

The ECIL 9 Organization Committee
Johan Maertens, Thierry Calandra, Simone Cesaro, Catherine Cordonnier, Rafael de la Camara, Peter Donnelly, Hermann Einsele, Raoul Herbrecht, Hans H. Hirsch, Per Ljungman, Georg Maschmeyer, Malgorzata Mikulska, Livio Pagano and

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Leukemia; https://doi.org/10.1038/s41375-022-01556-7

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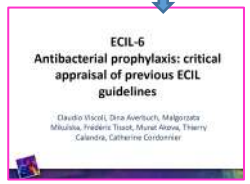

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Leukemia; https://doi.org/10.1038/s41375-022-01556-7

Table 2. Summary of drug characteristics, reported infectious complications and ECIL clinical practice recommendations for targeted drugs and biotherapies in acute leukemia.

Class of agents	Agent	Impact on immune system	Infectious events	ECIL recommendations
Anti-CD22 antibody-drug conjugate	Inotuzumab ozogamicin	No documented mechanism of immunosuppression	When combined with chemotherapy: febrile neutropenia, sepsis, pneumonia	• No specific antimicrobial prophylaxis (A-IIr) • No specific recommendation with the use of this drug in case of infection or fever • Special attention when combining this drug with other agents prolonging QT interval, such as levofloxacin or posaconazole (A-IIr)
Anti-CD33 antibody-drug conjugate	Gemtuzumab ozogamicin	No specific impact on immune defense except neutropenia	When given in combination with chemotherapy: febrile neutropenia, pneumonia, sepsis, fungal infection)	Recommended diagnostic procedures: • Standard of care in AML and neutropenic fever and/or infections (A-IIr) Treatment recommendations: • Standard of care in neutropenic fever and/or infections (A-IIr) Recommendations for prophylaxis: • Standard of care in AML, when given in combination (A-IIr) or high-dose GO for relapse (A-IIr) • No systemic antimicrobial prophylaxis when given as monotherapy (A-IIr) Recommendations on how to handle the drug in case of infection or fever: • Most infections occur subsequent to GO application, therefore no recommendation General recommendation • Careful monitoring of hepatotoxicity (A-I)
CD123 x CD3 bispecific dual-affinity retargeting antibody (DART)	Flotetuzumab	No documented mechanism of immunosuppression	No specific risks of infection in patients on flotetuzumab monotherapy	Recommended diagnostic procedures: • Standard of care in AML and neutropenic fever and/or infections (A-IIr) Treatment recommendations: • Standard of care in neutropenic fever and/or infections (A-IIr) Recommendations for prophylaxis: • No specific recommendation due to lack of data when given as monotherapy Recommendations on how to handle the drug in case of infection: • No specific recommendation due to lack of data when given as monotherapy
Isocitrate dehydrogenase (IDH)-1 and -2 inhibitors	Enasidenib, ivosidenib, olutasidenib	No documented mechanism of immunosuppression	Reports on severe differentiation syndrome which may mimic an infection (fever, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusion, hyperleukocytosis, renal impairment, multiorgan failure)	Recommended diagnostic procedures: • Standard of care in AML and neutropenic fever and/or infections (A-IIr) Treatment recommendations: • Standard of care in neutropenic fever and/or infections (A-IIr) Recommendations for prophylaxis: • No systemic antimicrobial prophylaxis when given as monotherapy (A-IIr) Recommendations on how to handle the drug in case of infection: • No specific recommendations
FLT3-Tyrosine Kinase Inhibitor, also active against receptor tyrosine kinases KIT and AXL	Gilteritinib	No documented mechanism of immunosuppression	Infections in relapsed and/or refractory AML patients on gilteritinib: febrile neutropenia, sepsis pneumonia	Recommended diagnostic procedures: • Standard of care in AML and neutropenic fever and/or infections (A-IIr) Treatment recommendations: • Standard of care in neutropenic fever and/or infections (A-IIr) Recommendations for prophylaxis: • No systemic antimicrobial prophylaxis when given as monotherapy (A-IIr)

ECIL-9 (Eylül 2021)

Leukemia www.nature.com/leu

REVIEW ARTICLE OPEN

Infectious complications of targeted drugs and biotherapies in acute leukemia. Clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL), a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and the European Leukemia Net (ELN)

Georg Maschmeyer[1], Lars Bullinger[2], Carolina Garcia-Vidal[3], Raoul Herbrecht[4], Johan Maertens[5], Pierantonio Menna[6], Livio Pagano[7], Anne Thiebaut-Bertrand[8] and Thierry Calandra[9]

Leukemia

Table 2. Summary of drug characteristics, reported infectious complications and ECIL clinical practice recommendations for targeted drugs and biotherapies in acute leukemia.

Class of agents	Agent	Impact on immune system	Infectious events	ECIL recommendations
Anti-CD22 antibody-drug conjugate	Inotuzumab ozogamicin	No documented mechanism of immunosuppression	When combined with chemotherapy: febrile neutropenia, sepsis, pneumonia	• No specific antimicrobial prophylaxis (A-III) • No specific recommendation with the use of this drug in case of infection or fever • Special attention when combining this drug with other agents prolonging QT interval, such as levofloxacin or posaconazole (A-III)
Anti-CD33 antibody-drug conjugate	Gemtuzumab ozogamicin	No specific impact on immune defense except neutropenia	When given in combination with chemotherapy: febrile neutropenia, pneumonia, sepsis, fungal infection)	Recommended diagnostic procedures: • Standard of care in AML and neutropenic fever and/or infections (A-III) Treatment recommendations: • Standard of care in neutropenic fever and/or infections (A-III) Recommendations for prophylaxis: • Standard of care in AML, when given in combination (A-III) or high-dose GO for relapse (A-III) • No systemic antimicrobial prophylaxis when given as monotherapy (A-III) Recommendations on how to handle the drug in case of infection or fever: • Most infections occur subsequent to GO application, therefore no recommendation General recommendation • Careful monitoring of hepatotoxicity (A-II

IDSA'nın Febril Nötropeni Rehberi ne diyor?

PERFORMANCE MEASURES

1. All patients with fever and neutropenia should be evaluated for level of risk (high or low), have history and physical examination performed, have cultures and radiological tests performed, and initiate treatment with broad-spectrum empirical antibiotics promptly (ie, within 2 h of presentation). In the absence of effector cells, primarily neutrophils, signs and symptoms of inflammation may be lacking and rapid progression of invasive bacterial infections may occur, so antibiotics are a life-saving measure in this situation. However, the collection of clinical and laboratory data that will locate a potential site or cause of infection is critical prior to the initiation of antibiotics.
2. Antimicrobial changes or additions to the initial empirical antibiotic regimen should be based on clinical, radiographic, or microbiological evidence of infection and not on the persistence of fever alone in a patient whose condition is otherwise stable. An exception is that empirical antifungal therapy should be started after 4–7 days of fever that does not respond to empirical antibiotic therapy.
3. Low-risk patients who are anticipated to have a short duration of neutropenia (<7 days) do not require antibiotic prophylaxis.

IDSA GUIDELINES

Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

Michigan Üniversitesi- Hematoloji Hastalarında Profilaksi Rehberi

MICHIGAN MEDICINE
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PROPHYLAXIS GUIDELINES FOR THE ADULT HEMATOLOGY PATIENT

	Indication	Antibacterial	Antifungal	PJP prophylaxis	Antiviral	Duration of Prophylaxis
MDS	Receiving chemotherapy	No routine prophylaxis	Fluconazole 200 mg PO daily	*No routine prophylaxis*	Acyclovir 400 mg PO BID	Antifungal: Beginning when ANC ≤500 and continuing throughout neutropenia Antiviral: Throughout all chemotherapy cycles
AML	APL Induction	No routine prophylaxis *If differentiating on steroids:* Levofloxacin 500 mg PO daily	Micafungin 100 mg IV q24h	No routine prophylaxis	Acyclovir 400 mg PO BID	Antibacterial/Antifungal: If indicated begin when ANC ≤500 and continuing throughout neutropenia. In consolidation send Rx for patient to start at discharge continue throughout neutropenia PCP: Throughout all chemotherapy cycles. Continued for 6 mo following last dose of purine analogue. Antiviral: Throughout all chemotherapy cycles
	AML Intensive Induction	No routine prophylaxis	Voriconazole 200 mg PO BID (trough level after 5-7 days)	*For patients receiving purine analogue[4]* TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	
	HMA + Venetoclax	Levofloxacin 500 mg PO daily	Posaconazole 300 mg tab PO daily			
	Relapsed/Refractory or ≥70 years Induction	Levofloxacin 500 mg PO daily	*For relapsed/refractory patients unlikely to recover ANC:* Posaconazole 300 mg tab PO daily			
	Consolidation	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily			
ALL	ALL Induction	Levofloxacin 500 mg PO daily	Micafungin 50 mg IV q24h	TMP-SMX (Bactrim) DS 3 times weekly (hold through methotrexate admission until level <0.1 µM)	Acyclovir 400 mg PO BID	
	Beyond Induction	No routine prophylaxis *For patients receiving HyperCVAD:* Levofloxacin 500 mg PO daily	*For patients receiving HyperCVAD:* Fluconazole 200 mg PO daily			
	Blinatumomab	No routine prophylaxis *If prolonged neutropenia:* Levofloxacin 500 mg PO daily	No routine prophylaxis *If prolonged neutropenia:* Posaconazole 300 mg tab PO daily			
	Inotuzumab	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily			
	Hairy Cell Leukemia	Levofloxacin 500 mg PO daily	*If no G-CSF support being used* Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Antibacterial/Antifungal: Beginning when ANC ≤500 and continuing throughout neutropenia PCP: Throughout all chemotherapy cycles. Continued for 6 mo following last dose of purine analogue. Antiviral: Throughout all chemotherapy cycles
	Aplastic Anemia	*If neutropenic on discharge:* Levofloxacin 500 mg PO daily	*If neutropenic on discharge:* Voriconazole 200 mg PO BID[1] (trough level after 5-7 days)	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID EBV/CMV monitoring	Antibacterial/Antifungal: Beginning when ANC ≤500 and continuing throughout neutropenia PCP: Beginning with therapy and continuing for at least 6 mo Antiviral: Throughout all therapy

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	Indication	Antibacterial	Antifungal	PJP prophylaxis	Antiviral	Duration of Prophylaxis
Myeloma	High dose steroids[3]	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	Proteasome inhibitors (e.g., bortezomib, carfilzomib, ixazomib)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles and continuing for at least 3 months post last dose
	Monoclonal antibodies (e.g., Elotuzumab, isatuximab, daratumumab)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles and continuing for at least 3 months post last dose
	VDT-PACE or DCEP	Levofloxacin 500mg daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Antifungal/Antibacterial: Send Rx for patient to start at discharge and continue throughout neutropenia PCP/Antiviral: Throughout all chemotherapy cycles
Lymphoma	BEACOPP	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	DA-R-EPOCH HIV Negative	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	DA-R-EPOCH HIV Positive[4]	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Antifungal/Antibacterial: Send Rx for patient to start at discharge and continue throughout neutropenia. For outpatient EPOCH, start on day 6. PCP/Antiviral: Throughout all chemotherapy cycles
	HyperCVAD CODOX-M/IVAC	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly (hold through methotrexate admission until level <0.1 µM)	Acyclovir 400 mg PO BID	Antibacterial: Beginning with Part B of regimen and continued throughout all chemotherapy cycles Antifungal: Send Rx for patient to start at discharge and continue throughout neutropenia PCP/Antiviral: Throughout all chemotherapy cycles
	R-ICE, R-ESHAP, R-DHAP Nordic	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	PI3K inhibitor (e.g., idelalisib, copanlisib, duvelisib)	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	No routine prophylaxis CMV monitoring	PCP: Through duration of treatment
	Purine analogues (cladribine, fludarabine, nelarabine, pentostatin, bendamustine)	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	PCP: Beginning with chemotherapy and continued at least 6 months after treatment and until normalization of ALC (≥1.2 k/uL) Antiviral: Throughout all chemotherapy cycles
	Alemtuzumab	No routine prophylaxis	Voriconazole 200 mg PO BID	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID EBV/CMV monitoring	Antifungal: Beginning when ANC ≤500 and continuing throughout neutropenia PCP/Antiviral: Beginning with therapy and continued 6 mo after therapy or until normalization of ALC (≥1.2 k/uL)
	Maintenance Anti-CD20 (e.g., rituximab, obinutuzumab)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg BID Hepatitis B screen prior to initiation	Throughout all chemotherapy cycles

Stanford Üniversitesi- Hematoloji Hastalarında Profilaksi Rehberi

Stanford HEALTH CARE

Stanford Antimicrobial Safety and Sustainability Program

Antimicrobial Prophylaxis in Hematology/Oncology Patients Admitted to Stanford Health Care

	Antibacterial	Antifungal	Antiviral	PJP
General Considerations	• ANC <500 cells/mm^3 for >7 days • Weigh risks of prolonged antimicrobial exposure (e.g. MDRO colonization, *C. difficile* infection, etc.)	• ANC <500 cells/mm^3 for >7 days • Mucositis (increased candidiasis risk) • >10% risk of candidiasis • Consider mold-active prophylaxis when >6-8% risk of aspergillosis	• HSV or VZV seropositive • Prior HSV or VZV episode • T-cell suppression • Prolonged neutropenia • Mucositis	• >3.5% risk of developing PJP • T-cell suppression (especially CD4 <200 cells/mm^3)
Utility	Reduce risk of bacteremia and fever Potential mortality benefit	Reduce risk of fungal infection and related mortality	Reduce risk of viral reactivation	Reduce risk of PJP infection and related mortality
Agents *Preferred*	Levofloxacin	Fluconazole (candida prophylaxis only) Posaconazole (mold-active prophylaxis)	Acyclovir	TMP/SMX
Alternative	If intolerance, contraindication, or allergy to fluoroquinolone: cefpodoxime	If drug interaction, intolerance, or contraindication (consider spectrum indicated): caspofungin, isavuconazole, liposomal amphotericin B, voriconazole	If patient preference: famciclovir, valacyclovir	If drug interaction, intolerance, allergy, or contraindication to TMP/SMX: atovaquone, dapsone, inhaled pentamidine
AML *Induction*	Consider during neutropenia	Posaconazole during neutropenia	During treatment course	Consider if purine analog (see section below)
Consolidation or low-intensity treatment	No routine prophylaxis	Consider posaconazole if ANC <500 cells/mm^3 >7 days		
ALL *Induction through maintenance*	Consider during neutropenia	Fluconazole or caspofungin during neutropenia (see appendix for spectrum)	During treatment course	During treatment course
Blinatumomab (for relapsed/refractory ALL)	No routine prophylaxis	Consider mold-active prophylaxis based on duration and depth of neutropenia	Consider during treatment course	Consider during treatment course
Lymphoma *Most regimens*	No routine prophylaxis	No routine prophylaxis	Consider during treatment course	No routine prophylaxis, consider if prolonged CD4 <200 cells/mm^3
Intensive chemotherapy (e.g. R-CODOX-M/R-IVAC, HyperCVAD)	Consider during neutropenia	Consider fluconazole during neutropenia		
MT-R for PCNSL	No routine prophylaxis	No routine prophylaxis		During treatment course (avoid TMP/SMX during HD-MTX)
Multiple Myeloma *Proteasome inhibitors*	No routine prophylaxis	No routine prophylaxis	During treatment course	No routine prophylaxis
Daratumumab			During treatment course and 3 months after	
Intensive chemotherapy (e.g. VTE-PACE)	Consider during neutropenia	Consider fluconazole during neutropenia	Consider during treatment course	

Original Date: 12/10/2020 **ICHS Committee approved:** 09/14/2020 **ABX Subcommittee approved:** 09/17/2020 **Hematology/Oncology Faculty approved:** 12/11/2020
Authors: Edna Cheung, PharmD BCOP; William Alegria, PharmD BCIDP Gabriel Mannis, MD

Stanford Antimicrobial Safety and Sustainability Program

(continued from above)	Antibacterial	Antifungal	Antiviral	PJP
High-dose Steroids	No routine prophylaxis	Mold-active prophylaxis if ≥ 1 mg/kg/day prednisone equivalents for 2 weeks (threshold not well defined, consider patient-specific risk factors)	Consider during treatment course (threshold not well defined, increased risk with ≥ 10 mg/day prednisone equivalents)	Prophylaxis if ≥ 20 mg/day prednisone equivalents for 4 weeks
Purine Analogs *(fludarabine, cladribine, clofarabine, pentostatin)*	No routine prophylaxis	Consider mold-active prophylaxis if ANC <500 cells/mm^3 for >7 days	Consider during treatment course	Consider during treatment course (especially if CD4 <200 cells/mm^3), may consider continuing up to 6 months after treatment (consider patient-specific risk factors)

Considerations for specific treatments

Treatment Agent	Prophylaxis	Additional Monitoring
Alemtuzumab	HSV and PJP prophylaxis until minimum of 2 months after treatment and CD4 > 200 cells/mm^3	CMV surveillance
BTK inhibitors (e.g. ibrutinib)	No routine prophylaxis, generally higher infection risk in first 6 months Consider VZV and PJP prophylaxis (assess patient-specific risk factors)	Consider differential diagnoses (viral, bacterial, fungal, PJP) if clinical suspicion for infection
PI3K inhibitors (e.g. idelalisib)	Consider PJP prophylaxis	CMV surveillance

Abbreviations: ANC = absolute neutrophil count, HD-MTX = high-dose methotrexate, HSV = Herpes simplex virus, MDRO = multi-drug resistant organisms, MT-R = high-dose methotrexate with temozolomide and rituximab, PJP = Pneumocystis jirovecii pneumonia, TMP/SMX = trimethoprim/sulfamethoxazole, VZV = Varicella zoster virus

Farklı öneriler ve uygulamalar var

MICHIGAN MEDICINE
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	Indication	Antibacterial	Antifungal	PJP prophylaxis	Antiviral	Duration of Prophylaxis
Myeloma	High dose steroids[3]	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	Proteasome inhibitors (e.g., bortezomib, carfilzomib, ixazomib)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles and continuing for at least 3 months post last dose
	Monoclonal antibodies (e.g., Elotuzumab, isatuximab, daratumumab)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles and continuing for at least 3 months post last dose
	VDT-PACE or DCEP	Levofloxacin 500mg daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Antifungal/Antibacterial: Send Rx for patient to start at discharge and continue throughout neutropenia PCP/Antiviral: Throughout all chemotherapy cycles
Lymphoma	BEACOPP	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	DA-R-EPOCH HIV Negative	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	DA-R-EPOCH HIV Positive[4]	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	Antifungal/Antibacterial: Send Rx for patient to start at discharge and continue throughout neutropenia. For outpatient EPOCH, start on day 6. PCP/Antiviral: Throughout all chemotherapy cycles
	HyperCVAD CODOX-M/IVAC	Levofloxacin 500 mg PO daily	Fluconazole 200 mg PO daily	TMP-SMX (Bactrim) DS 3 times weekly (hold through methotrexate admission until level <0.1 µM)	Acyclovir 400 mg PO BID	Antibacterial: Beginning with Part B of regimen and continued throughout all chemotherapy cycles Antifungal: Send Rx for patient to start at discharge and continue throughout neutropenia PCP/Antiviral: Throughout all chemotherapy cycles
	R-ICE, R-ESHAP, R-DHAP Nordic	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg PO BID	Throughout all chemotherapy cycles
	PI3K inhibitor (e.g., idelalisib, copanlisib, duvelisib)	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	No routine prophylaxis CMV monitoring	PCP: Through duration of treatment
	Purine analogues (cladribine, fludarabine, nelarabine, pentostatin, bendamustine)	No routine prophylaxis	No routine prophylaxis	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID	PCP: Beginning with chemotherapy and continued at least 6 months after treatment and until normalization of ALC (≥1.2 k/uL) Antiviral: Throughout all chemotherapy cycles
	Alemtuzumab	No routine prophylaxis	Voriconazole 200 mg PO BID	TMP-SMX (Bactrim) DS 3 times weekly	Acyclovir 400 mg PO BID EBV/CMV monitoring	Antifungal: Beginning when ANC ≤500 and continuing throughout neutropenia PCP/Antiviral: Beginning with therapy and continued 6 mo after therapy or until normalization of ALC (≥1.2 k/uL)
	Maintenance Anti-CD20 (e.g., rituximab, obinutuzumab)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis	Acyclovir 400 mg BID Hepatitis B screen prior to initiation	Throughout all chemotherapy cycles

Stanford Antimicrobial Safety and Sustainability Program

(continued from above)	Antibacterial	Antifungal	Antiviral	PJP
High-dose Steroids	No routine prophylaxis	Mold-active prophylaxis if ≥ 1 mg/kg/day prednisone equivalents for 2 weeks (threshold not well defined, consider patient-specific risk factors)	Consider during treatment course (threshold not well defined, increased risk with ≥ 10 mg/day prednisone equivalents)	Prophylaxis if ≥ 20 mg/day prednisone equivalents for 4 weeks
Purine Analogs *(fludarabine, cladribine, clofarabine, pentostatin)*	No routine prophylaxis	Consider mold-active prophylaxis if ANC <500 cells/mm^3 for >7 days	Consider during treatment course	Consider during treatment course (especially if CD4 <200 cells/mm^3), may consider continuing up to 6 months after treatment (consider patient-specific risk factors)

Considerations for specific treatments

Treatment Agent	Prophylaxis	Additional Monitoring
Alemtuzumab	HSV and PJP prophylaxis until minimum of 2 months after treatment and CD4 > 200 cells/mm^3	CMV surveillance
BTK inhibitors (e.g. ibrutinib)	No routine prophylaxis, generally higher infection risk in first 6 months Consider VZV and PJP prophylaxis (assess patient-specific risk factors)	Consider differential diagnoses (viral, bacterial, fungal, PJP) if clinical suspicion for infection
PI3K inhibitors (e.g. idelalisib)	Consider PJP prophylaxis	CMV surveillance

Abbreviations: ANC = absolute neutrophil count, HD-MTX = high-dose methotrexate, HSV = Herpes simplex virus, MDRO = multi-drug resistant organisms, MT-R = high-dose methotrexate with temozolomide and rituximab, PJP = Pneumocystis jirovecii pneumonia, TMP/SMX = trimethoprim/sulfamethoxazole, VZV = Varicella zoster virus

Stanford'da Genel Yaklaşım

Stanford HEALTH CARE

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Utility	Reduce risk of bacteremia and fever Potential mortality benefit	Reduce risk of fungal infection and related mortality	Reduce risk of viral reactivation	Reduce risk of PJP infection and related mortality
Agents *Preferred*	Levofloxacin	Fluconazole (candida prophylaxis only) Posaconazole (mold-active prophylaxis)	Acyclovir	TMP/SMX
Alternative	If intolerance, contraindication, or allergy to fluoroquinolone: cefpodoxime	If drug interaction, intolerance, or contraindication (consider spectrum indicated): caspofungin, isavuconazole, liposomal amphotericin B, voriconazole	If patient preference: famciclovir, valacyclovir	If drug interaction, intolerance, allergy, or contraindication to TMP/SMX: atovaquone, dapsone, inhaled pentamidine

Anti-bakteriyel profilaksi

Journal of Infection (2018) 76, 20–37

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Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines

Malgorzata Mikulska [a,*], Diana Averbuch [1,b], Frederic Tissot [1,c], Catherine Cordonnier [d], Murat Akova [e], Thierry Calandra [f], Marcello Ceppi [g], Paolo Bruzzi [g], Claudio Viscoli [a] on behalf of the European Conference on Infections in Leukemia (ECIL), a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and the European Leukemia Net (ELN)

First objective: assessment of the efficacy of FQ prophylaxis

Two aspects of FQ prophylaxis were considered, i.e. its direct efficacy in reducing infection-related outcomes (see below) and if there was evidence of a decreased efficacy related to increased FQ resistance.

Second objective: impact of FQ prophylaxis on antibiotic resistance

In order to fully evaluate the benefits and risks of FQ prophylaxis, its potential impact on the selection of resistant strains and on inducing resistance was assessed. A systematic review of data from the identified studies was performed with the aim of describing the rate of colonisation or BSI due to FQ resistant and multidrug resistant bacteria in the groups with and without FQ prophylaxis. In order to report absolute and not relative changes in antibiotic resistance, the denominator for the rate of colonisation and infection due to resistant bacteria was the number of patients included in the study and not the number of pathogens isolated in surveillance swabs or blood cultures. Additionally, data from the meta-analysis focusing exclusively on FQ resistance were reported.[19]

Anti-bakteriyel profilaksi

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Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines

Summary *Objectives:* Fluoroquinolone (FQ) prophylaxis was recommended in 2005 by European Conference on Infections in Leukemia (ECIL) for patients with prolonged neutropenia. In consideration of a worldwide increase in antibiotic resistance, the issue of FQ prophylaxis during neutropenia was re-evaluated.

Methods: Literature review of randomised controlled trials (RCT) and observational studies published in years 2006–2014 was performed. Their results were analysed in meta-analysis. Meta-regression model was applied to evaluate whether the rates of FQ resistance in community and hospital settings influenced the efficacy of FQ prophylaxis. The impact of FQ prophylaxis on colonisation and infection with resistant bacteria was reviewed.

Results: Two RCTs and 12 observational studies were identified. FQ prophylaxis did not have effect on mortality (pooled OR 1.01, 95%CI 0.73–1.41), but was associated with lower rate of bloodstream infections (BSI) (pooled OR 0.57, 95%CI 0.43–0.74) and episodes of fever during neutropenia (pooled OR 0.32, 95%CI 0.20–0.50). No effect of the background rate of FQ resistance on the efficacy of FQ prophylaxis was observed. In few studies, FQ prophylaxis resulted in an increased colonisation or infection with FQ- or multi-drug resistant strains.

Conclusions: The possible benefits of FQ prophylaxis on BSI rate, but not on overall mortality, should be weighed against its impact in terms of toxicity and changes in local ecology in single centres.

- Antibakteriyel profilakside çoğunlukla levofloksasin kullanılıyor
- Daha az sıklıkta siprofloksasin kullanılıyor
- Ateş ataklarını ve bakteremiyi azaltıyor ancak mortaliteyi etkilemiyor
- Direnç sorunu mutlaka gözönünde bulundurulmalı

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Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines

Last but not least, ethical issues of withdrawing FQ prophylaxis should be considered, since it is still recommended by most of the guidelines. Interestingly, based on the same data from the literature, only the Australian and ESMO guidelines put the extensive use of FQ in the context of increasing antibiotic resistance, and, considering no benefit on mortality, advised against the routine use of FQ prophylaxis during neutropenia.[25,30]

Although this review found no data contradicting the ECIL 1 recommendation on FQ prophylaxis administered in order to prevent infections in neutropenic patients, two main caveats need to be considered. First, antibiotic pressure has been invariably linked to an increase in bacterial resistance which has already an important negative impact worldwide. Second, the potential benefit of lower rate of BSI is limited, has no evident impact on mortality and, most importantly, was demonstrated only in settings with low or moderate resistance rates and, as such, cannot be held applicable to regions with a high prevalence of resistant pathogens. Therefore, local antibiotic policies on FQ use should be in line with national antimicrobial stewardship programs and based on local epidemiological data, although no clear cut off guaranteeing the efficacy of FQ prophylaxis could be provided.[88] The world- f a global crisis in terms of antimicrobial read of MDR pathogens, calls for changes in at indications that were apparently consolidated and for new responsibilities of every specialist concerning proper use of antibiotics.[89,90]

- Etik kaygılar da önemli
- Profilaksi kararı ulusal/yerel düzeyde değerlendirilmeli

clinical practice guidelines

Annals of Oncology 27 (Supplement 5): v111–v118, 2016
doi:10.1093/annonc/mdw325

Management of febrile neutropaenia: ESMO Clinical Practice Guidelines†

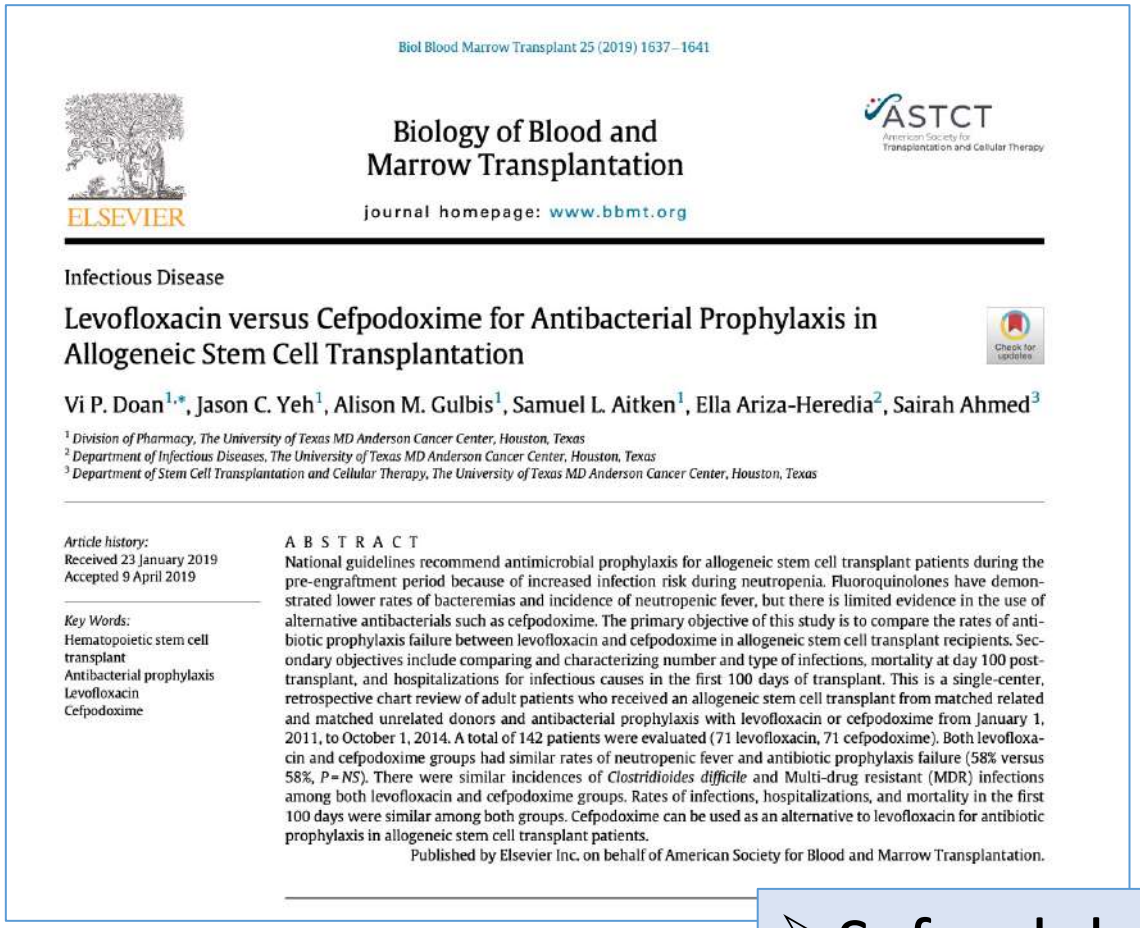
J. Klastersky[1], J. de Naurois[2], K. Rolston[3], B. Rapoport[4], G. Maschmeyer[5], M. Aapro[6] & J. Herrstedt[7] on behalf of the ESMO Guidelines Committee*

[1]*Institut Jules Bordet—Centre des Tumeurs de l'ULB, Brussels, Belgium;* [2]*St Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, UK;* [3]*M.D. Anderson Cancer Center, Houston, TX, USA;* [4]*Medical Oncology Centre of Rosebank, Johannesburg, South Africa;* [5]*Department of Hematology, Oncology and Palliative Care, Ernst von Bergmann Hospital, Potsdam, Germany;* [6]*Multidisciplinary Institute of Oncology, Clinique de Genolier, Genolier, Switzerland;* [7]*Department of Oncology, Odense University Hospital (OUH), Odense, Denmark*

chemoprophylaxis

Antimicrobials (first non-absorbable antibiotics and later, co-trimoxazole) have been used for a long time for the prevention of episodes of FN in ChT-treated patients. This approach has been somewhat successful, but has also led to the emergence of resistant strains, limiting its efficacy. Since the 1990s, fluoroquinolones have been used extensively for chemoprophylaxis. Most studies have shown that fluoroquinolones reduce the incidence of infection and, in some studies, also the infection-related mortality, but at the expense of the emergence of quinolone-resistant strains. This should, in the end, render the prophylaxis useless; moreover, these strains jeopardise the use of fluoroquinolones as a therapy of FN in low-risk patients, as will be discussed elsewhere. For all of these reasons, the use of antimicrobials, including fluoroquinolones, should be discouraged. Guidelines from the EORTC (European Organisation for Research and Treatment of Cancer) and American Society of Clinical Oncology (ASCO) recommend that clinicians limit the use of antibacterial prophylaxis to patients at high risk for FN; others recommend the mere avoidance of such practices for the prevention of FN. The most recent update of the Cochrane meta-analysis still recommended the use of ciprofloxacin or levofloxacin in cancer patients undergoing intensive ChT [4].

Anti-bakteriyel profilaksi



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Infectious Disease

Levofloxacin versus Cefpodoxime for Antibacterial Prophylaxis in Allogeneic Stem Cell Transplantation

Vi P. Doan[1,*], Jason C. Yeh[1], Alison M. Gulbis[1], Samuel L. Aitken[1], Ella Ariza-Heredia[2], Sairah Ahmed[3]

[1] Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, Texas
[2] Department of Infectious Diseases, The University of Texas MD Anderson Cancer Center, Houston, Texas
[3] Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, Texas

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ABSTRACT

National guidelines recommend antimicrobial prophylaxis for allogeneic stem cell transplant patients during the pre-engraftment period because of increased infection risk during neutropenia. Fluoroquinolones have demonstrated lower rates of bacteremias and incidence of neutropenic fever, but there is limited evidence in the use of alternative antibacterials such as cefpodoxime. The primary objective of this study is to compare the rates of antibiotic prophylaxis failure between levofloxacin and cefpodoxime in allogeneic stem cell transplant recipients. Secondary objectives include comparing and characterizing number and type of infections, mortality at day 100 post-transplant, and hospitalizations for infectious causes in the first 100 days of transplant. This is a single-center, retrospective chart review of adult patients who received an allogeneic stem cell transplant from matched related and matched unrelated donors and antibacterial prophylaxis with levofloxacin or cefpodoxime from January 1, 2011, to October 1, 2014. A total of 142 patients were evaluated (71 levofloxacin, 71 cefpodoxime). Both levofloxacin and cefpodoxime groups had similar rates of neutropenic fever and antibiotic prophylaxis failure (58% versus 58%, *P* = *NS*). There were similar incidences of *Clostridioides difficile* and Multi-drug resistant (MDR) infections among both levofloxacin and cefpodoxime groups. Rates of infections, hospitalizations, and mortality in the first 100 days were similar among both groups. Cefpodoxime can be used as an alternative to levofloxacin for antibiotic prophylaxis in allogeneic stem cell transplant patients.

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➢Sefpodoksim de levofloksasin kadar etkili bulunmuş

Anti-bakteriyel profilaksi

Stanford HEALTH CARE

Antimicrobial Prophylaxis in Hema

	Antibacterial
General Considerations	• ANC <500 cells/mm³ for >7 days • Weigh risks of prolonged antimicrobial exposure (e.g. MDRO colonization, *C. difficile* infection, etc.)
Utility	Reduce risk of bacteremia and fever Potential mortality benefit
Agents	Levofloxacin
Preferred	
Alternative	If intolerance, contraindication, or allergy to fluoroquinolone: cefpodoxime
AML	Consider during neutropenia
Induction	
Consolidation or low-intensity treatment	No routine prophylaxis
ALL	Consider during neutropenia
Induction through maintenance	
Blinatumomab (for relapsed/refractory ALL)	No routine prophylaxis
Lymphoma	No routine prophylaxis
Most regimens	
Intensive chemotherapy (e.g. R-CODOX-M/R-IVAC, HyperCVAD)	Consider during neutropenia
MT-R for PCNSL	No routine prophylaxis
Multiple Myeloma	No routine prophylaxis
Proteasome inhibitors	
Daratumumab	
Intensive chemotherapy (e.g. VTE-PACE)	Consider during neutropenia
High-dose Steroids	No routine prophylaxis
Purine Analogs *(fludarabine, cladribine, clofarabine, pentostatin)*	No routine prophylaxis

- Nötropeni süresi 7 günden uzun olacak hastalar için öneriliyor
- Antibakteriyel profilakside levofloksasin öneriliyor
- Direnç sorunu mutlaka gözönünde bulundurulmalı

Levofloksasin dışındaki seçenekler

Stanford Antimicrobial Safety and Sustainability Program

Appendix: Overview of Antimicrobial Prophylaxis Treatment Agents

- Listed in alphabetical order; please see above for choice of agent
- For more information, please refer to SHC Antimicrobial Dosing Reference Guide and SHC Antifungal Therapeutic Drug Monitoring Guide

Antibacterial Prophylaxis

Agent	Spectrum	Dosing	Dose Adjustment	CYP Drug Interactions	Adverse Effects
Cefdinir	Similar to cefpodoxime	300 mg PO BID	Renal	None	Generally well tolerated
Cefpodoxime	Similar to levofloxacin, except no *P. aeruginosa* activity	200 mg PO BID	Renal	None	Generally well tolerated
Ciprofloxacin	Similar to levofloxacin, except less Gram-positive activity	500 – 750 mg PO BID or 400 mg IV BID – TID	Renal	Inhibits 1A2 (moderate)	Similar to levofloxacin
Levofloxacin	Active against Gram-negative Enterobacteriaceae, Streptococcal spp, atypical organisms, P. aeruginosa	500 – 750 mg PO or IV daily	Renal	None	Photosensitivity, rash, prolonged QTc, C. difficile, CNS effects (headache, dizziness), arthralgias, tendinitis, peripheral neuropathy, dysglycemia

Anti-bakteriyel profilaksiye ilişkin

- Nötropeni süresi 7 günden uzun olacak hastalar için öneriliyor
- Antibakteriyel profilakside çoğunlukla levofloksasin kullanılıyor
- Siprofloksasin, sefpodoksim ve sefdinir levofloksasine alternatif olarak düşünülebilir
- Ateş ataklarını ve bakteremiyi azaltıyor ancak mortaliteyi etkilemiyor
- Direnç sorunu mutlaka göz önünde bulundurulmalı

Anti-fungal profilaksi

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9th European Conference on Infections in Leukaemia

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Resources

ECIL 9 Part 2 - Revised Guidelines

- Update on Hepatitis B, C and E - revised guidelines
- Toxoplasmosis/Toxoplasma infection and disease - final recommendations (pdf file)
- Update on fungal diagnostics - revised guidelines
- Update on COVID 19 in Hematology-Oncology patients
  - Epidemiology and risk factors - final recommendations (pdf file)
  - Viral biology and diagnosis - revised guidelines
  - Clinical symptoms and infection control - final recommendations (pdf file)
  - Therapy - final recommendations (pdf file)
  - Vaccine - final recommendations (pdf file)

List of ECIL 9 on-site attendees

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Covid19 in Hemathology-Oncology patients

- Epidemiology and risk factors - final recommendations (pdf file)
- Viral biology and diagnosis - final recommendations (pdf file)
- Clinical symptoms and infection control - final recommendations (pdf file)
- Therapy - final recommendations (pdf file)
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- Update on Fungal and Bacterial Infections Group - (pediatric antifungal guidelines) - final slide set
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  - Influenza Virus - final slide set
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  - EBV management in patients with (leukemia and other hematological disorders - final slide set
  - CMV and HHV-6 management in patients with hematological diseases - final slide set
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- Antifungal prophylaxis - final slide set
- Antifungal treatment of Aspergillus and Candida infections - final slide set
- Management of herpes virus infections
  - HSV - final slide set
  - VZV - final slide set
  - CMV, HHV-6,7,8 - final slide set
  - EBV - final slide set
- Management of other viral infections
  - Respiratory Viruses. Influenza Virus
  - Polyoma, Parainfluenza virus

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- Empirical antifungal treatment for persistent fever in neutropenic patients - final slide set
- Antifungal prophylaxis - final slide set
- Antifungal therapy - final slide set

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REVIEW ARTICLE OPEN

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Infectious complications of targeted drugs and biotherapies in acute leukemia. Clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL), a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and the European Leukemia Net (ELN)

Georg Maschmeyer[1✉], Lars Bullinger[2], Carolina Garcia-Vidal[3], Raoul Herbrecht[4], Johan Maertens[5], Pierantonio Menna[6], Livio Pagano[7], Anne Thiebaut-Bertrand[8] and Thierry Calandra[9]

The 9th web-based European Conference on Infections in Leukemia (ECIL-9), held September 16-17, 2021, reviewed the risk of infections and febrile neutropenia associated with more recently approved immunotherapeutic agents and molecular targeted drugs for the treatment of acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). Novel antibody based treatment approaches (inotuzumab ozogamicin, gemtuzumab ozogamicin, flotetuzumab), isocitrate dehydrogenases inhibitors (ivosidenib, enasidenib, olutasidenib), FLT3 kinase inhibitors (gilteritinib, midostaurin, quizartinib), a hedgehog inhibitor (glasdegib) as well as a BCL2 inhibitor (venetoclax) were reviewed with respect to their mode of action, their immunosuppressive potential, their current approval and the infectious complications and febrile neutropenia reported from clinical studies. Evidence-based recommendations for prevention and management of infectious complications and specific alerts regarding the potential for drug-drug interactions were developed and discussed in a plenary session with the panel of experts until consensus was reached. The set of recommendations was posted on the ECIL website for a month for comments from members of EBMT, EORTC, ICHS and ELN before final approval by the panelists. While a majority of these agents are not associated with a significantly increased risk when used as monotherapy, caution is required with combination therapy such as venetoclax plus hypomethylating agents, gemtuzumab ozogamicin plus cytotoxic drugs or midostaurin added to conventional AML chemotherapy.

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Journal of Antimicrobial Chemotherapy

European guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommendations from the European Conference on Infections in Leukaemia

KLİMİK Kongresi, 2023

Anti-fungal profilaksi

J Antimicrob Chemother 2018; 73: 3221–3230
doi:10.1093/jac/dky286 Advance Access publication 1 August 2018

Journal of Antimicrobial Chemotherapy

European guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommendations from the European Conference on Infections in Leukaemia

Johan A. Maertens[1]*, Corrado Girmenia[2], Roger J. Brüggemann[3], Rafael F. Duarte[4], Christopher C. Kibbler[5], Per Ljungman[6], Zdeněk Racil[7], Patricia Ribaud[8], Monica A. Slavin[9,10], Oliver A. Cornely[11–13], J. Peter Donnelly[14] and Catherine Cordonnier[15,16] on behalf of the European Conference on Infections in Leukaemia (ECIL)†, a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the Immunocompromised Host Society (ICHS) and the European LeukemiaNet (ELN)

[1]Department of Haematology, Universitaire Ziekenhuizen Leuven, Leuven, Belgium; [2]Department of Haematology, Azienda Policlinico Umberto I, Sapienza University of Rome, Rome, Italy; [3]Department of Pharmacy, Radboud University Medical Centre, Nijmegen, The Netherlands; [4]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [5]Centre for Medical Microbiology, University College London, London, UK; [6]Departments of Haematology and Allogeneic Stem Cell Transplantation, Karolinska University Hospital and Division of Haematology, Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden; [7]Department of Internal Medicine – Haematology and Oncology, Masaryk University and University Hospital Brno, Brno, Czech Republic; [8]Quality Unit, Pôle PréBloc, Saint-Louis and Lariboisière Hospital Group, Assistance Publique-Hôpitaux de Paris, Paris, France; [9]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Victorian Comprehensive Cancer Centre, Melbourne, Australia; [10]Department of Medicine, University of Melbourne, Parkville, Victoria, Australia; [11]Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Cologne, Germany; [12]Clinical Trials Centre Cologne (ZKS Köln), Cologne, Germany; [13]Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany; [14]Department of Haematology, Radboud University Medical Centre, Nijmegen, The Netherlands; [15]Hopital Henri Mondor, Assistance Publique-Hôpitaux de Paris, Department of Haematology, Créteil, France; [16]Université Paris-Est-Créteil, Créteil, France

*Corresponding author. Tel: +3216346889; Fax: +3216346881; E-mail: johan.maertens@uzleuven.be
†Participants in the ECIL-5 and -6 meetings are listed in the Acknowledgements.

AML and recipients of an allogeneic HSCT. In fact, due to new therapeutic approaches including biotherapies, IFD has recently been reported more frequently in many haematological diseases, including lymphoproliferative disorders.[5] Hence, the group considered it useful for the haematology community to extend its analysis and recommendations for primary antifungal prophylaxis in these populations. Of note, separate guidelines on antifungal prophylaxis for patients with aplastic anaemia have been recently published by the aplastic anaemia working party of the EBMT.[6] Also recently, specific guidelines on the use of biomarkers for diagnosis of IFD,[7] the prevention of infections due to *Pneumocystis jirovecii*[8] and the management of IFD in the paediatric population[4] have been published elsewhere.

Introduction

In 2005, the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the European LeukemiaNet (ELN) and the International Immunocompromised Host Society (ICHS) inaugurated the European Conference on Infections in Leukaemia (ECIL). Its main goal was to elaborate guidelines or recommendations for the management of infections due to bacteria, viruses and fungi among leukaemia patients as well as those undergoing haematopoietic stem cell transplantation (HSCT) and to identify unmet needs and areas for further research.[1] The prevention of invasive fungal disease (IFD) has been one of the key topics from the beginning.[1,2] Since 2006, all proposed guidelines

Anti-fungal profilaksi-Kök hücre nakli

Autologous HSCT

Patients undergoing autologous HSCT, for whatever underlying condition, are at low risk of IFD. Primary antifungal prophylaxis is not recommended, although fluconazole (400 mg q24h) should be considered to prevent mucosal *Candida* infection during the neutropenic phase (B-III).[50–53]

Allogeneic HSCT

Post-engraftment period (Table 5)

Given the significantly increased risk of invasive mould infection during GvHD (and its associated high mortality), we strongly recommend against the use of fluconazole for prophylaxis in patients with high-risk GvHD (A-III).

Based on the results of a large, double-blind study, posaconazole (oral solution or gastroresistant tablet/iv formulation) is the drug of choice for antifungal prophylaxis (A-I).[59] However, no difference is observed in patients with (limited or extensive) chronic GvHD.[59]

Pre-engraftment period (Table 4)

Fluconazole (400 mg/day) is still recommended for centres with a low incidence of mould infections (i.e. below 5%, the reported incidence in allogeneic HSCT in the PIMDA audit[21]) but only when combined with a mould-directed diagnostic approach (biomarker and/or CT scan-based) or a mould-directed therapeutic approach (empirical antifungal therapy) (A-I).[33] Centres with a higher incidence of mould infections should adopt an alternative approach (A-III).

Anti-fungal profilaksi

Table 3. ECIL recommendations on primary antifungal prophylaxis in adult patients with AML and MDS undergoing intensive remission-induction chemotherapy[a]

Antifungal agent	Grading	Comments
Posaconazole oral solution 200 mg q8h *or* tablet 300 mg q24h following a loading dose of 300 mg q12h on day 1	A-I	Recommended if baseline incidence of mould infections is high. Given the increased absorption of the tablet, it is likely that the need for therapeutic drug monitoring will become restricted to specific populations (e.g. severe mucositis).
Fluconazole 400 mg q24h	B-I	Only recommended if the incidence of mould infections is low. Fluconazole may be part of an integrated care strategy together with a mould-directed diagnostic approach.
Itraconazole oral solution 2.5 mg/kg q12h	B-I	Recommended if baseline incidence of mould infections is high. May be limited by drug–drug interactions or patient tolerability. It is recommended to monitor serum drug concentrations.
Voriconazole 200 mg q12h	B-II	Recommended if baseline incidence of mould infections is high. It is recommended to monitor serum drug concentrations.
All echinocandins	C-II	Insufficient data on efficacy and tolerability.
Liposomal amphotericin B	C-II	Insufficient data on dose, frequency and duration, as well as on efficacy and tolerability.
Lipid-associated amphotericin B	C-II	Insufficient data on dose, frequency and duration, as well as on efficacy and tolerability.
Aerosolized liposomal amphotericin B (10 mg twice weekly)	B-I	Only when combined with fluconazole 400 mg q24h.
Amphotericin B deoxycholate	A-II against	
Aerosolized amphotericin B deoxycholate	A-I against	

[a]Primary antifungal prophylaxis might be considered during intensified consolidation therapy (see text).

AML ve MDS olgularının remisyon-indüksiyonu sırasında **posakonazol**

J Antimicrob Chemother 2018; **73**: 3221–3230
doi:10.1093/jac/dky286 Advance Access publication 1 August 2018

Journal of Antimicrobial Chemotherapy

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Anti-fungal profilaksi

Table 4. ECIL recommendations on primary antifungal prophylaxis in adult allogeneic HSCT recipients: pre-engraftment period

	Pre-engraftment risk of mould infections	
Antifungal agent	low	high
Fluconazole 400 mg q24h	A-I	
Posaconazole oral solution 200 mg q8h *or* tablet 300 mg q24h following a loading dose of 300 mg q12h on day 1	B-II	B-II
Itraconazole oral solution 2.5 mg/kg q12h	B-I	B-I
Voriconazole 200 mg q12h	B-I	B-I
Micafungin 50 mg q24h	B-I	C-I
Caspofungin and anidulafungin	no data	no data
Liposomal amphotericin B	C-II	C-II
Aerosolized liposomal amphotericin B (10 mg twice weekly) plus fluconazole 400 mg q24h	C-III	B-II
Fluconazole 400 mg q24h		A-III against

Allojeneik kemik iliği naklinde engarfman **öncesi flukonazol**

Table 5. ECIL recommendations on primary antifungal prophylaxis in adult allogeneic HSCT recipients: post-engraftment period

Antifungal agent	High risk GvHD
Posaconazole oral solution 200 mg q8h *or* tablet 300 mg q24h following a loading dose of 300 mg q12h on day 1	A-I[a,b]
Itraconazole oral solution 2.5 mg/kg q12h	B-I[b]
Voriconazole 200 mg q12h	B-I[b]
Micafungin 50 mg q24h	C-II
Caspofungin and anidulafungin	no data
Liposomal amphotericin B	C-II
Aerosolized liposomal amphotericin B (10 mg twice weekly) plus fluconazole 400 mg q24h	no data
Fluconazole 400 mg q24h	A-III against

[a]No difference with placebo was seen in patients with chronic GvHD.[59]
[b]It is recommended to monitor serum drug concentrations.

Allojeneik kemik iliği naklinde engarfman **sonrası posakonazol**

Anti-fungal profilaksi

Vorikonazol, Mucorales'e etkili DEĞİL!

Antifungal Prophylaxis

Agent	Spectrum	Dosing	Dose Adjustment	CYP Drug Interactions	Adverse Effects
Caspofungin	• Active against Candida spp • Some activity against Aspergillus spp • Not active against dimorphic fungi, Mucorales, Cryptococcus spp.	70 mg IV x1 load, then 50 mg daily	None	None	Well tolerated
Fluconazole	• Active against most Candida spp; variable activity against C. glabrata; no activity against C. krusei • Active against Coccidioides, Cryptococcus spp	400 mg PO/IV daily	Renal	Inhibits 3A4 (moderate), 2C9 (moderate), 2C19 (strong)	Well tolerated, increased LFTs
Isavuconazole	Similar to posaconazole	372 mg PO/IV q8h x6 load, then 372 mg daily	None	Inhibits 3A4 (moderate) Substrate of 3A4	Similar to posaconazole, except shortens QTc
Liposomal amphotericin B	• Broad-spectrum antifungal activity • Not active against A. terreus, Candida lusitaniae, Lomentospora	3-5 mg/kg IV daily (adjusted body weight in obese)	None	None	AKI, hypokalemia, hypomagnesemia, infusion reactions (fever, chills, rigors, hypotension)
Posaconazole	• Active against Candida spp, Aspergillus spp • Some activity against Mucorales, Cryptococcus spp, dimorphic fungi	300 mg PO/IV q12h x2 load, then 300 mg daily*	None	Inhibits CYP3A4 (strong)	Increased LFTs, prolonged QTc, headache, rash, hypokalemia
Voriconazole	• Similar to posaconazole, except not active against Mucorales • Preferred agent for Scedosporium	400 mg PO q12h x2 load, then 200 mg q12h** 6 mg/kg IV q12h x2 load, then 4 mg/kg q12h (AdjBW in obese) **	Hepatic No renal dose adjustment	Inhibits CYP3A4 (strong), 2C19 (moderate) Substrate of CYP 2C19	Visual disturbances, hallucinations, photosensitivity, rash, increased LFTs, prolonged QTc, rare cases of skin malignancies (long-term use)

*Oral delayed-release tablet preferred and taken with food (oral suspension: not interchangeable with tablets, interpatient variability, consider therapeutic drug monitoring)
**Therapeutic drug monitoring recommended for all patients

Original Date: 12/10/2020 **ICHS Committee approved:** 09/14/2020 **ABX Subcommittee approved:** 09/17/2020 **Hematology/Oncology Faculty approved:** 12/11/2020
Authors: Edna Cheung, PharmD BCOP; William Alegria, PharmD BCIDP Gabriel Mannis, MD

Anti-fungal profilaksi- Hedefe yönelik ilaçlar ve biyoterapiler

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REVIEW ARTICLE OPEN

Infectious complications of targeted drugs and biotherapies in acute leukemia. Clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL), a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and the European Leukemia Net (ELN)

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Leukemia; https://doi.org/10.1038/s41375-022-01556-7

INTRODUCTION

For several decades, intensive combination chemotherapy, with or without hematopoietic cell transplantation, has been the backbone for the treatment of acute leukemia in younger and fit patients, whereas less toxic regimes (e.g., use of hypomethylating agents) have been used in older and unfit patients. However, over the past 10–15 years, tremendous progress has been made in deciphering the molecular pathogenesis and phenotypic diversity of acute leukemia. Several intracellular signaling pathways that are critical to the genesis of this disease have been identified. This new knowledge has also revealed various immunological and molecular therapeutic targets, paving the way for precision medicine approaches, both for acute myeloid leukemia and acute lymphoblastic leukemia. Recently, several small-molecule inhibitors and immunotherapies have been successfully introduced, either as single agents or in combination with standard-of-care

[1]Certified Cancer Center, Klinikum Ernst von Bergmann, Charlottenstrasse 72, D-14467 Potsdam, Germany. [2]Department of Hematology, Oncology and Tumor Immunology, Campus Virchow, Charité – Universitätsmedizin Berlin, German Cancer Consortium (DKTK), Partner Site Berlin, Berlin, Germany. [3]Infectious Diseases Department, Hospital Clinic-IDIBAPS, Villarroel 170, BCN 08036 Barcelona, Spain. [4]Department of Hematology, Institut de Cancérologie Strasbourg Europe (ICANS) and Université de Strasbourg, Inserm, UMR-S 1113/IRFAC, Strasbourg, France. [5]Department of Hematology, Immunology, and Transplantation, KU Leuven, Leuven and Department of Hematology, UZ Leuven, Leuven, Belgium. [6]Department of Sciences and Technologies for Humans and the Environment, University Campus Bio-Medico of Rome, University Hospital Foundation Campus Bio-Medico of Rome, Rome, Italy. [7]Hematology Division, Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli – IRCCS and Università Cattolica del Sacro Cuore, Rome, Italy. [8]Department of Hematology, Grenoble University Hospital, Grenoble, France. [9]Infectious Diseases Service, Department of Medicine, Lausanne University Hospital, University of Lausanne, CH-1011 Lausanne, Switzerland. ✉email: gm-kl@gmx.de

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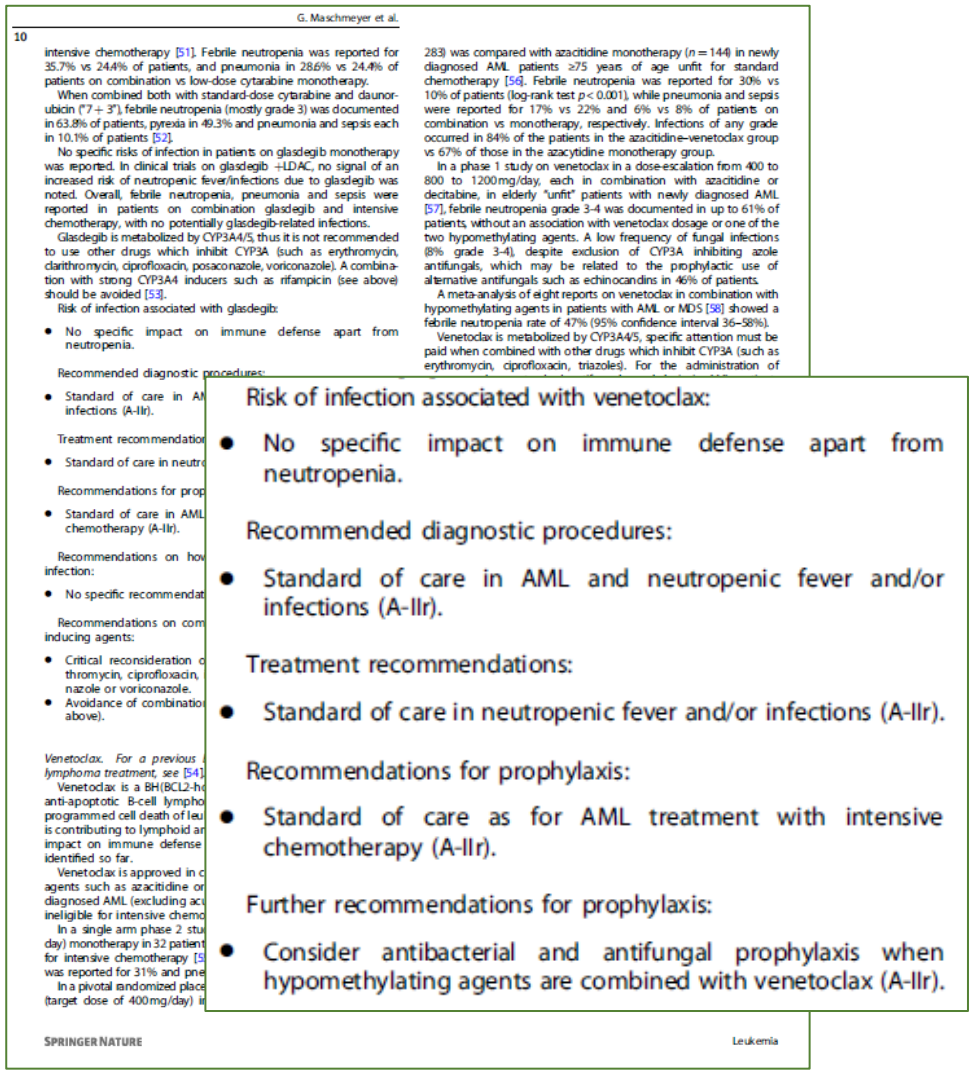


intensive chemotherapy [51]. Febrile neutropenia was reported for 35.7% vs 24.4% of patients, and pneumonia in 28.6% vs 24.4% of patients on combination vs low-dose cytarabine monotherapy.

When combined both with standard-dose cytarabine and daunorubicin ("7 + 3"), febrile neutropenia (mostly grade 3) was documented in 63.8% of patients, pyrexia in 49.3% and pneumonia and sepsis each in 10.1% of patients [52].

No specific risks of infection in patients on glasdegib monotherapy was reported. In clinical trials on glasdegib +LDAC, no signal of an increased risk of neutropenic fever/infections due to glasdegib was noted. Overall, febrile neutropenia, pneumonia and sepsis were reported in patients on combination glasdegib and intensive chemotherapy, with no potentially glasdegib-related infections.

Glasdegib is metabolized by CYP3A4/5, thus it is not recommended to use other drugs which inhibit CYP3A (such as erythromycin, clarithromycin, ciprofloxacin, posaconazole, voriconazole). A combination with strong CYP3A4 inducers such as rifampicin (see above) should be avoided [53].

Risk of infection associated with glasdegib:

- No specific impact on immune defense apart from neutropenia.

Recommended diagnostic procedures:

- Standard of care in A infections (A-IIr).

Treatment recommendatio

- Standard of care in neutr

Recommendations for prop

- Standard of care in AML chemotherapy (A-IIr).

Recommendations on ho infection:

- No specific recommendat

Recommendations on com inducing agents:

- Critical reconsideration o thromycin, ciprofloxacin, nazole or voriconazole.
- Avoidance of combinatio above).

Venetoclax. For a previous lymphoma treatment, see [54]

Venetoclax is a BH(BCL2-ho anti-apoptotic B-cell lympho programmed cell death of leu is contributing to lymphoid ar impact on immune defense identified so far.

Venetoclax is approved in c agents such as azacitidine or diagnosed AML (excluding ac ineligible for intensive chemo

In a single arm phase 2 stu day) monotherapy in 32 patient for intensive chemotherapy [5 was reported for 31% and pne

In a pivotal randomized place (target dose of 400 mg/day) i

283) was compared with azacitidine monotherapy ($n = 144$) in newly diagnosed AML patients ≥75 years of age unfit for standard chemotherapy [56]. Febrile neutropenia was reported for 30% vs 10% of patients (log-rank test $p < 0.001$), while pneumonia and sepsis were reported for 17% vs 22% and 6% vs 8% of patients on combination vs monotherapy, respectively. Infections of any grade occurred in 84% of the patients in the azacitidine–venetoclax group vs 67% of those in the azacytidine monotherapy group.

In a phase 1 study on venetoclax in a dose-escalation from 400 to 800 to 1200 mg/day, each in combination with azacitidine or decitabine, in elderly "unfit" patients with newly diagnosed AML [57], febrile neutropenia grade 3-4 was documented in up to 61% of patients, without an association with venetoclax dosage or one of the two hypomethylating agents. A low frequency of fungal infections (8% grade 3-4), despite exclusion of CYP3A inhibiting azole antifungals, which may be related to the prophylactic use of alternative antifungals such as echinocandins in 46% of patients.

A meta-analysis of eight reports on venetoclax in combination with hypomethylating agents in patients with AML or MDS [58] showed a febrile neutropenia rate of 47% (95% confidence interval 36–58%).

Venetoclax is metabolized by CYP3A4/5, specific attention must be paid when combined with other drugs which inhibit CYP3A (such as erythromycin, ciprofloxacin, triazoles). For the administration of

Risk of infection associated with venetoclax:

- No specific impact on immune defense apart from neutropenia.

Recommended diagnostic procedures:

- Standard of care in AML and neutropenic fever and/or infections (A-IIr).

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr).

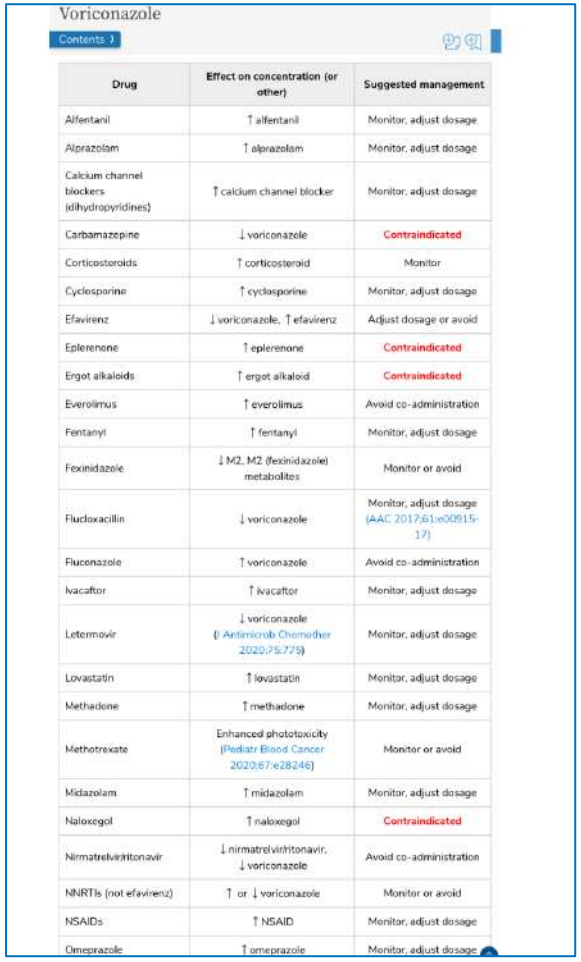
Recommendations for prophylaxis:

- Standard of care as for AML treatment with intensive chemotherapy (A-IIr).

Further recommendations for prophylaxis:

- Consider antibacterial and antifungal prophylaxis when hypomethylating agents are combined with venetoclax (A-IIr).

İlaç etkileşimleri mutlaka kontrol edilmeli!



Voriconazole

Contents

Drug	Effect on concentration (or other)	Suggested management
Alfentanil	↑ alfentanil	Monitor, adjust dosage
Alprazolam	↑ alprazolam	Monitor, adjust dosage
Calcium channel blockers (dihydropyridines)	↑ calcium channel blocker	Monitor, adjust dosage
Carbamazepine	↓ voriconazole	Contraindicated
Corticosteroids	↑ corticosteroid	Monitor
Cyclosporine	↑ cyclosporine	Monitor, adjust dosage
Efavirenz	↓ voriconazole, ↑ efavirenz	Adjust dosage or avoid
Eplerenone	↑ eplerenone	Contraindicated
Ergot alkaloids	↑ ergot alkaloid	Contraindicated
Everolimus	↑ everolimus	Avoid co-administration
Fentanyl	↑ fentanyl	Monitor, adjust dosage
Fexinidazole	↓ M2, M2 (fexinidazole) metabolites	Monitor or avoid
Flucloxacillin	↓ voriconazole	Monitor, adjust dosage (AAC 2017;61:e00915-17)
Fluconazole	↑ voriconazole	Avoid co-administration
Ivacaftor	↑ ivacaftor	Monitor, adjust dosage
Letermovir	↓ voriconazole (J Antimicrob Chemother 2020;75:775)	Monitor, adjust dosage
Lovastatin	↑ lovastatin	Monitor, adjust dosage
Methadone	↑ methadone	Monitor, adjust dosage
Methotrexate	Enhanced phototoxicity (Pediatr Blood Cancer 2020;67:e28246)	Monitor or avoid
Midazolam	↑ midazolam	Monitor, adjust dosage
Naloxegol	↑ naloxegol	Contraindicated
Nirmatrelvir/ritonavir	↓ nirmatrelvir/ritonavir, ↓ voriconazole	Avoid co-administration
NNRTIs (not efavirenz)	↑ or ↓ voriconazole	Monitor or avoid
NSAIDs	↑ NSAID	Monitor, adjust dosage
Omeprazole	↑ omeprazole	Monitor, adjust dosage

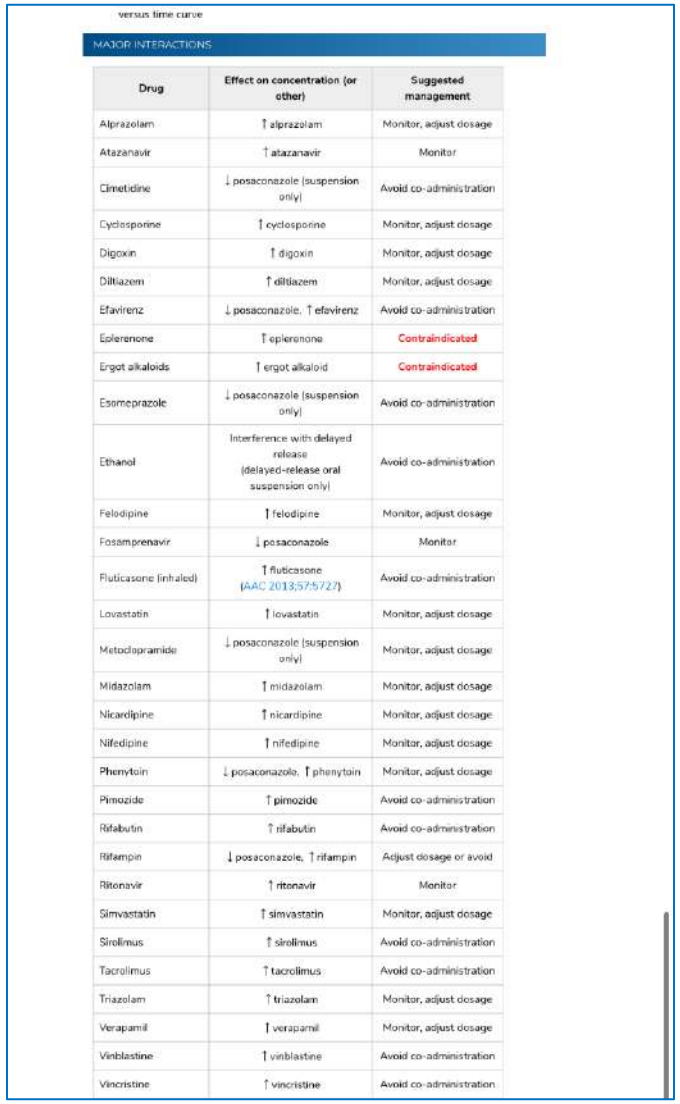
Interactions between your drugs

Major **voriconazole ⇄ ibrutinib**

Applies to: voriconazole, ibrutinib

Talk to your doctor before using ibrutinib together with voriconazole. Combining these medications may significantly increase the blood levels of ibrutinib. This may increase the risk of side effects such as nausea, vomiting, diarrhea, abdominal pain, constipation, hemorrhage, kidney problems, and impaired bone marrow function resulting in low numbers of different types of blood cells. You may also be more likely to develop anemia, bleeding problems, or infections due to low blood cell counts. You may need a dose adjustment or more frequent monitoring to safely use both medications, or you may be advised by your doctor to interrupt or delay treatment with ibrutinib until after you are done with voriconazole therapy, if feasible. Your doctor may also be able to prescribe alternatives that do not interact. You should contact your doctor if you develop paleness, fatigue, dizziness, fainting, unusual bruising or bleeding, fever, chills, diarrhea, sore throat, muscle aches, shortness of breath, blood in phlegm, weight loss, red or inflamed skin, body sores, and pain or burning during urination. Also seek immediate medical attention if you experience signs and symptoms that may suggest kidney damage such as nausea, vomiting, loss of appetite, increased or decreased urination, sudden weight gain or weight loss, fluid retention, swelling, shortness of breath, muscle cramps, tiredness, weakness, dizziness, confusion, and irregular heart rhythm. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

İlaç etkileşimleri mutlaka kontrol edilmeli!



versus time curve

MAJOR INTERACTIONS

Drug	Effect on concentration (or other)	Suggested management
Alprazolam	↑ alprazolam	Monitor, adjust dosage
Atazanavir	↑ atazanavir	Monitor
Cimetidine	↓ posaconazole (suspension only)	Avoid co-administration
Cyclosporine	↑ cyclosporine	Monitor, adjust dosage
Digoxin	↑ digoxin	Monitor, adjust dosage
Diltiazem	↑ diltiazem	Monitor, adjust dosage
Efavirenz	↓ posaconazole, ↑ efavirenz	Avoid co-administration
Eplerenone	↑ eplerenone	Contraindicated
Ergot alkaloids	↑ ergot alkaloid	Contraindicated
Esomeprazole	↓ posaconazole (suspension only)	Avoid co-administration
Ethanol	Interference with delayed release (delayed-release oral suspension only)	Avoid co-administration
Felodipine	↑ felodipine	Monitor, adjust dosage
Fosamprenavir	↓ posaconazole	Monitor
Fluticasone (inhaled)	↑ fluticasone (AAC 2013;57:5727)	Avoid co-administration
Lovastatin	↑ lovastatin	Monitor, adjust dosage
Metoclopramide	↓ posaconazole (suspension only)	Monitor, adjust dosage
Midazolam	↑ midazolam	Monitor, adjust dosage
Nicardipine	↑ nicardipine	Monitor, adjust dosage
Nifedipine	↑ nifedipine	Monitor, adjust dosage
Phenytoin	↓ posaconazole, ↑ phenytoin	Monitor, adjust dosage
Pimozide	↑ pimozide	Avoid co-administration
Rifabutin	↑ rifabutin	Avoid co-administration
Rifampin	↓ posaconazole, ↑ rifampin	Adjust dosage or avoid
Ritonavir	↑ ritonavir	Monitor
Simvastatin	↑ simvastatin	Monitor, adjust dosage
Sirolimus	↑ sirolimus	Avoid co-administration
Tacrolimus	↑ tacrolimus	Avoid co-administration
Triazolam	↑ triazolam	Monitor, adjust dosage
Verapamil	↑ verapamil	Monitor, adjust dosage
Vinblastine	↑ vinblastine	Avoid co-administration
Vincristine	↑ vincristine	Avoid co-administration

Interactions between your drugs

Major **posaconazole ⇄ venetoclax**

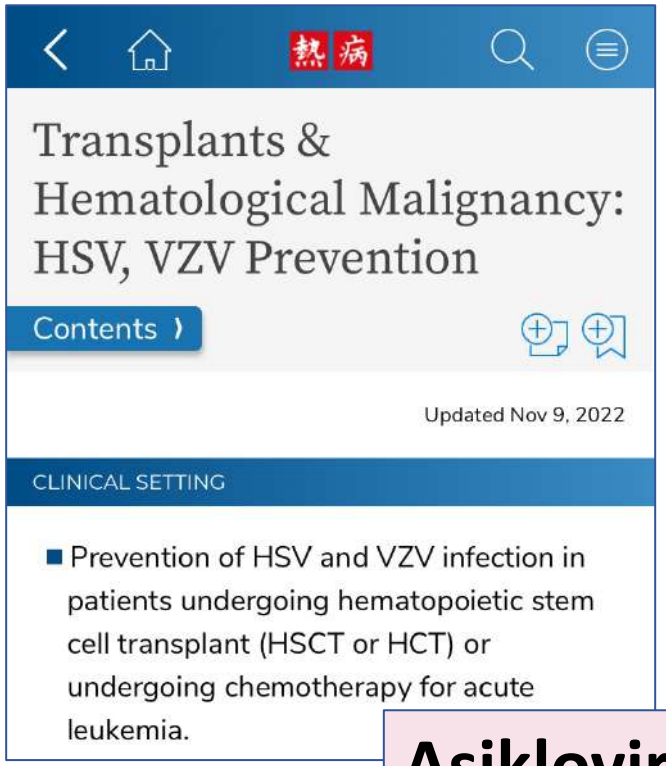
Applies to: posaconazole, venetoclax

Using venetoclax together with posaconazole is generally not recommended. Combining these medications may significantly increase the blood levels and effects of venetoclax. This may increase your risk of developing tumor lysis syndrome, a serious condition that is caused by the rapid breakdown of cancer cells and that can lead to kidney failure and even death. In addition, you may be more likely to experience other side effects such as nausea; vomiting; diarrhea; fatigue; and impaired bone marrow function resulting in low numbers of different types of blood cells, which can increase the risk of anemia, bleeding problems, and infections. Talk to your doctor if you have any questions or concerns. Your doctor may be able to prescribe alternatives that do not interact, or you may need a dose adjustment or more frequent monitoring to safely use both medications. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

Anti-fungal profilaksiye ilişkin

- Kandidiyazise örneğin allojeneik nakil öncesi flukonazol
- Küflere yönelik olarak allojeneik nakil sonrası posakonazol
- Serum ilaç düzeyi takibi önemli
- Antifungal profilaksi altında fungal enfeksiyon gelişebilir!
- İlaç etkileşimlerine dikkat!

HSV/VZV Profilaksisi



Transplants & Hematological Malignancy: HSV, VZV Prevention

Contents

Updated Nov 9, 2022

CLINICAL SETTING

- Prevention of HSV and VZV infection in patients undergoing hematopoietic stem cell transplant (HSCT or HCT) or undergoing chemotherapy for acute leukemia.

PRIMARY REGIMENS

- Hematologic malignancy and HCT: indications and duration
  - Acute leukemia undergoing chemotherapy: During neutropenia
  - Autologous HCT: During neutropenia and 30 days post HCT
  - Allogeneic HCT: During neutropenia and for at least 1 year post HCT
    - Acyclovir 800 mg po bid or 400 mg po 3-4x/day

ALTERNATIVE REGIMENS

- Valacyclovir 500 mg po 2-3x/day
- Famciclovir 250 mg po 2x/day

COMMENTS

- In allogeneic HCT recipients, consider Acyclovir prophylaxis for > 1 year if GVHD is present to prevent VZV.

Asiklovir, 2x800 mg veya 3-4X400 mg

- ➢ Akut lösemi tedavisi sırasında, nötropeni süresi boyunca
- ➢ Otolog KHN sonrası bir ay boyunca ve nötropeni sırasında
- ➢ Allojeneik KHN sonrası bir yıl boyunca ve nötropeni sırasında

CMV

- Prevention of cytomegalovirus (CMV) as an opportunistic infection primarily in hematopoietic stem cell transplant (HSCT or HCT) patients receiving an allogeneic transplant.
- Risk factors for CMV disease in HCT recipients include being a CMV seropositive recipient (R+) of a CMV seronegative donor (D-); T-cell depleted or cord blood transplants; and graft versus host diseases (GVHD).
- Prevention strategies include both prophylaxis and preemptive therapy, preemptive therapy is used more commonly in this population.

- Preemptive Strategy:
  - Monitor weekly for CMV viremia by PCR (or antigenemia) for 3-6 months post transplant with consideration for more prolonged monitoring in patients at risk for late-onset CMV disease (chronic graft versus host disease (GVHD) requiring systemic treatment, patients receiving high-dose steroids, T-cell depleted or cord blood transplant recipients, and CD4 < 100 cells/mL).
  - Start treatment with identification of CMV viremia or antigenemia.
  - Treatment: Valganciclovir 900 mg po bid or Ganciclovir 5 mg/kg IV q12h until clearance of viremia, but for not less than 2 weeks. At that point of viremia clearance, either switch to secondary prophylaxis (below) or resume preemptive approach.

- Prophylaxis
  - Letermovir 480 mg IV or po q24h
  - Valganciclovir 900 mg po q24h (beginning post-engraftment):

ALTERNATIVE REGIMENS

- Preemptive Therapy
  - Foscarnet 90 mg/kg IV q12h
  - Cidofovir 5 mg/kg IV once weekly (given with probenecid)
- Prophylaxis (beginning post-engraftment):
  - Ganciclovir 5 mg/kg IV 5-7 days/week
  - Foscarnet 60 mg/kg IV tid x 7 days then 90-120 mg/kg IV once daily
  - Cidofovir 5 mg/kg IV every other week (given with probenecid)

P.jirovecii-Ko-trimoksazol kullanımı

Pneumocystis pneumonia, ...

Contents

- Patients at risk include:
  - HIV/AIDS patients with CD4 counts <200 cells/μL.
  - Solid organ and hematopoietic stem cell transplant recipients. In case-control study, post-transplant PJP associated with active CMV, allograft rejection, and termination of prophylaxis: Clin infect Dis 2019;68:1320
  - Cancer chemotherapy patients, especially those on high-dose steroid therapy (≥ 20 mg of daily Prednisone, or the equivalent, for over a month).
  - Selected rheumatologic diseases that require ≥ 20 mg Prednisone (or the equivalent) on a daily basis.

- Indications for primary prophylaxis/chronic suppression:
  - HIV/AIDS patients with CD4 count < 200 cells/μL
  - Any patient taking equivalent of ≥ 20 mg Prednisone/day for more than 1 month
  - Patients receiving Alemtuzumab (monoclonal antibody for CLL), Temozolomide (alkylating agent for astrocytoma therapy)
  - Hematopoietic and solid organ transplant recipients during immunosuppression
  - Patients given Fludarabine (purine analog used to treat hematologic malignancy)
  - Patients with Wegener's granulomatosis treated with Prednisone + cyclophosphamide

- Bir aydan uzun süredir 20 mg/gün veya daha fazla prednizon alanlar
- KLL için alemtuzumab alanlar
- HKHN hastaları
- Fludarabin alanlar
- ..

PJP profilaksisi

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

	Indication	PJP prophylaxis
Myeloma	High dose steroids[3]	TMP-SMX (Bactrim) DS 3 times weekly
	Proteasome inhibitors (e.g., bortezomib, carfilzomib, ixazomib)	No routine prophylaxis
	Monoclonal antibodies (e.g., Elotuzumab, isatuximab, daratumumab)	No routine prophylaxis
	VDT-PACE or DCEP	TMP-SMX (Bactrim) DS 3 times weekly
Lymphoma	BEACOPP	TMP-SMX (Bactrim) DS 3 times weekly
	DA-R-EPOCH HIV Negative	TMP-SMX (Bactrim) DS 3 times weekly
	DA-R-EPOCH HIV Positive[4]	TMP-SMX (Bactrim) DS 3 times weekly
	HyperCVAD CODOX-M/IVAC	TMP-SMX (Bactrim) DS 3 times weekly (hold through methotrexate admission until level <0.1 µM)
	R-ICE, R-ESHAP, R-DHAP Nordic	No routine prophylaxis
	PI3K inhibitor (e.g., idelalisib, copanlisib, duvelisib)	TMP-SMX (Bactrim) DS 3 times weekly
	Purine analogues (cladribine, fludarabine, nelarabine, pentostatin, bendamustine)	TMP-SMX (Bactrim) DS 3 times weekly
	Alemtuzumab	TMP-SMX (Bactrim) DS 3 times weekly
	Maintenance Anti-CD20 (e.g., rituximab, obinutuzumab)	No routine prophylaxis

Stanford HEALTH CARE

al Safety and Sustainability Program

Antimici Health Care

	PJP
General Considerations	• >3.5% risk of developing PJP • T-cell suppression (especially CD4 <200 cells/mm^3)
Utility	Reduce risk of PJP infection and related mortality
Agents	TMP/SMX
Preferred	
Alternative	If drug interaction, intolerance, allergy, or contraindication to TMP/SMX: atovaquone, dapsone, inhaled pentamidine
AML	Consider if purine analog (see section below)
Induction	
Consolidation or low-intensity treatment	
ALL	During treatment course
Induction through maintenance	
Blinatumomab (for relapsed/refractory ALL)	Consider during treatment course
Lymphoma	No routine prophylaxis, consider if prolonged CD4 <200 cells/mm^3
Most regimens	
Intensive chemotherapy (e.g. R-CODOX-M/R-IVAC, HyperCVAD)	
MT-R for PCNSL	During treatment course (avoid TMP/SMX during HD-MTX)
Multiple Myeloma	No routine prophylaxis
Proteasome inhibitors	
Daratumumab	
Intensive chemotherapy (e.g. VTE-PACE)	

Original Date: 12/10/2020 IC lty approved: 12/11/2020
Authors: Edna Cheung, Phar

Profilaktik amaçla ko-trimoksazol kullanımı

Her gün 1 SS tablet veya haftada 3 mgün 1DS (forte) tablet

PJP Prophylaxis

Agent	Spectrum	Dosing	Dose Adjustment	CYP Drug Interactions	Adverse Effects
Atovaquone	Active against PJP, T. gondii	1500 mg PO daily	None	None	Headache, increased LFTs
Dapsone	Active against PJP	100 mg PO daily	None	Substrate of 3A4	Hemolytic anemia, methemoglobinemia Avoid in patients with G6PD deficiency
Pentamidine	Active against PJP	300 mg inhaled every 4 weeks*	None	None	Bronchospasm, dyspnea, cough, dizziness
TMP/SMX	Active against PJP, T. gondii, Nocardia spp, L. monocytogenes Some activity (suboptimal at PJP prophylaxis dosing) against S. aureus, Gram-negative Enterobacteriaceae	1 SS PO daily or 1 DS three times per week	Renal	None	Rash, photosensitivity, hemolytic anemia (G6PD deficient) Less common at PJP prophylaxis dosing: myelosuppression, hyperkalemia, increased SCr or BUN, AKI, increased LFTs Avoid in patients with sulfa allergy or G6PD deficiency

*Avoid IV pentamidine for prophylaxis (risk of infusion reaction and pancreatitis)

Özetle

- Hastanın tanısına ve hangi ilaçları aldığına göre profilaksi yaklaşımı değişmektedir
- Profilaksi konusundaki karar, hastanın primer doktorları ile birlikte verilmelidir
- Profilaksi altında da enfeksiyon geliştiği (breakthrough enfeksiyon) akılda tutulmalıdır
- İlaç etkileşimleri mutlaka araştırılmalıdır
- Antimikrobiyal direnç sorunu gözardı edilmemelidir

1. cilt

2. cilt

3. cilt

2022’den itibaren yılda 4 sayı yayımlanıyor