

Primary antifungal prophylaxis in patients with hematologic neoplasms

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases

Publisher

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- [Conflict of interests](#)

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1 Summary

Immunosuppressed patients are at high risk for invasive fungal infections, especially after intensive chemotherapy for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) and after allogeneic stem cell transplantation. Despite advances in the treatment of invasive fungal infections in recent decades, they are still associated with substantial morbidity and mortality. Thus, for certain patient populations and clinical situations, there is a proven benefit of antifungal prophylaxis through clinical trials. More recent data lead to periodic changes in previous recommendations.

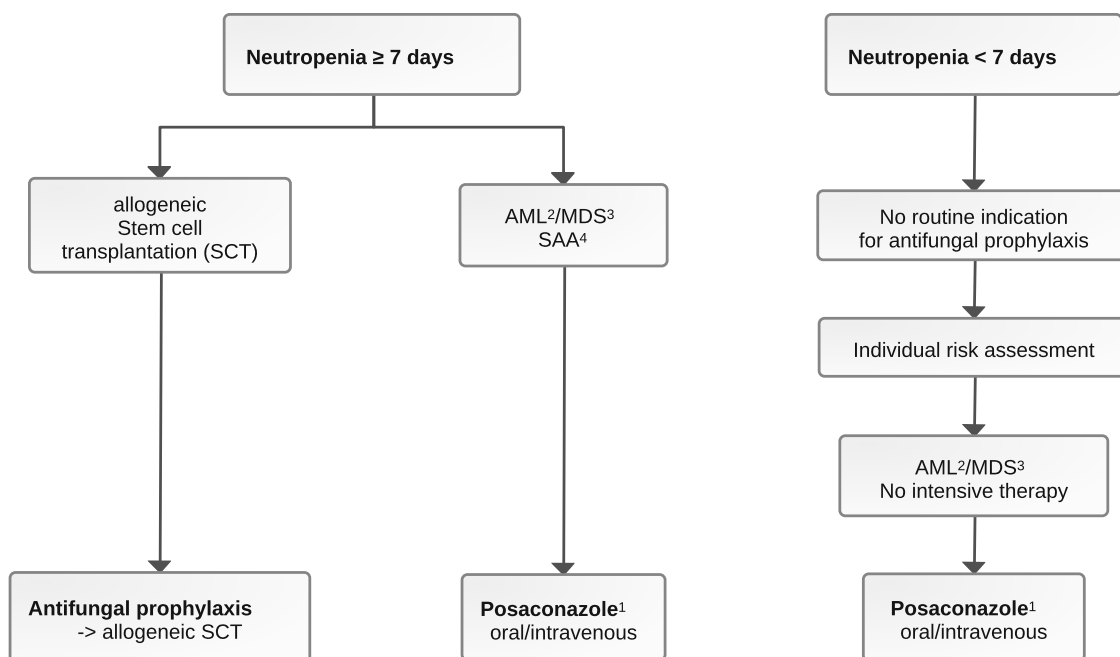
The guideline 'Antifungal primary prophylaxis in patients with hematologic neoplasms' was prepared by the Working Group on Infections of the DGHO (AGIHO) for the diagnosis and therapy of these patients [1]. It is based on a systematic literature search, a uniform assessment of the strength of evidence [2] and a consensus-building process. This is the summary of these recommendations.

6 Therapy

6.1 Therapy structure

The recommendations for antifungal prophylaxis in relation to the underlying disease and treatment are summarized in [Figure 1](#).

Figure 1: Antifungal prophylaxis in patients with hematologic neoplasms.



Legend:

¹ alternative antifungal agents with lower strength of evidence see [Table 1](#),

² acute myeloid leukemia,

³ myelodysplastic syndrome,

⁴ severe aplastic anemia

6.1.1 Prolonged neutropenia (<500 neutrophils/μl for ≥ 7 days) after therapy of hematologic neoplasms

Prolonged neutropenia was defined as <500 neutrophils/μl for ≥7 days. Data and recommendations are summarized in [Table 1](#). Patients after allogeneic stem cell transplantation were excluded [2].

Table 1: Recommendations for primary antifungal prophylaxis in patients with hematologic neoplasms with neutropenia ≥ 7 days.¹

Drug	Recommendation and evidence ¹ [2]
Posaconazole	A-I ² B-III ³
Amphotericin B, liposomal, inhalation	B-II
Amphotericin B, liposomal, iv	C-I
Caspofungin	C-I
Fluconazole	C-I
Itraconazole, p.o. + iv	C-I
SUBA itraconazole	C-II_{t,h}
Isavuconazole	B-II_t
Micafungin	B-II_{u, t}
Voriconazole	B-II_u
Amphotericin B, deoxycholate	D-I

Legend:

:

¹ Recommendations are not applicable to patients with ALL.

² strong recommendation for induction therapy of patients with AML/MDS.

³ vSAA, non-intensive therapy of MDS.

Table 2: Dosages of antifungal primary prophylaxis

Drug	Dosages	Drug monitoring (target mirror)	Recommendation and evidence [2]
Amphotericin B liposomal, inhalation	1. mg 2 times/week		
Amphotericin B liposomal, infusion solution	Recommended dose is not defined		
Anidulafungin	100 mg q24h i.v. (200 mg on day 1).		
Caspofungin, iv	50 mg q24h i.v. (70 mg on day 1, 70 mg also from day 2 if > 80 kg).		
Fluconazole, capsules	400 mg q24h p.o.		
Isavuconazole, iv	200 mg q24h (on day 1-2 q8h)		
Itraconazole, capsules	200 mg q24h p.o.		
Itraconazole, oral suspension	1. - 7.5 mg/kg or 200 mg q24h		
Itraconazole, iv	200 mg q24h i.v.		
SUBA - Itraconazole	200 mg q24h p.o.		
Micafungin, iv	50 mg q24h i.v.		
Posaconazole, oral suspension	200 mg q8h p.o. (2 times/day on day 1)	> 700 ng/ml	B-II_{t,u}
Posaconazole, tablets	300 mg q24h p.o. (2 times/day on day 1)	> 500 ng/ml	B-II_{t,u}
Posaconazole, iv	300 mg q24h i.v. (2 times/day on day 1)	> 500 ng/ml	B-II_{t,u}
Voriconazole	4 mg/kg q12h i.v./p.o.		B-II_{t,u}

Table 3: Recommendations for therapeutic drug monitoring

Substance	Rationale	Destination	SoR	QoE	Comment
All triazoles: In the event of a possible breakthrough IFI	description of therapeutic options	variable	A	III	
Oral itraconazole	Monitoring for efficacy and toxicity	>0.5 mg/L	B	II _t	
Isavuconazole	Monitoring in case of toxicity	2 - 5 mg/L	C	II _t	Higher concentrations are associated with increased toxicity
Posaconazole Oral suspension	Optimization of efficacy (even in case of reduced absorption)	>0.7 mg/L (prophylaxis) >1 mg/L (therapy)	B	II _t	Reduced plasma levels in GI-GvHD, diarrhea, PPI simultaneous.
Posaconazole p.o./i.v.	Optimization of efficacy		B	III	
Voriconazole	Optimization of efficacy	>1 mg/L	B	II _t	
Voriconazole	To avoid toxicity	<4.5 mg/L	A	II	Recommended in case of suspected toxicity

Table 4: Oral tumor therapy for AML/MDS and potential interactions with antifungals.

Therapy	Intention	Intervention	SoR	QoE
Venetoclax	Prophylaxis of invasive mycoses	Triazoles	A	II _{u,t}
	Reduction of interactions / toxicity	Dose reduction of venetoclax by at least 75% in combination with posaconazole or voriconazole and by 50% in combination with fluconazole or isavuconazole.	A	II _{u,t}
Gilteritinib	Prophylaxis of invasive mycoses	Triazoles, no dose adjustment necessary	A	II _u
Midostaurin	Prophylaxis of invasive mycoses	Triazoles, no dose adjustment necessary	A	II _{u,a}
Quizartinib	Prophylaxis of invasive mycoses	Triazoles, no dose adjustment necessary	A	II _{u,t}
	Reduction of interactions / toxicity	Dose reduction of quizartinib (60 to 30 mg or 30 mg to 20 mg) in combination with posaconazole or voriconazole.	B	III
Ivosidenib	Prophylaxis of invasive mycoses	Triazoles, no dose adjustment necessary	A	III
	Reduction of interactions / toxicity	Dose reduction ivosidenib to 250 mg/d in combination with posaconazole or voriconazole.	B	III

9 References

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16 Disclosure of Potential Conflicts of Interest

according to the rules of the responsible Medical Societies.