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Review

Antibacterial, antifungal and antiviral prophylaxis and vaccination strategies in adult patients with acute myeloid and promyelocytic leukemia: An expert panel consensus from the GIMEMA group

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ABSTRACT

Infections are a leading cause of morbidity, mortality, and treatment delays in AML and APL. While international guidelines emphasize intensive chemotherapy, they often overlook less intensive regimens, rely on outdated data, and ignore rising MDR infections. A GIMEMA survey across Italian centers revealed significant heterogeneity in antimicrobial prophylaxis, and vaccination practices. An expert panel reviewed 2012–2025 English literature with focus on infections via Delphi/nominal group methods, achieving ≥70% consensus. Prophylaxis with fluoroquinolones showed low agreement (28%) for intensive chemotherapy and venetoclax-based regimens due to no survival benefit, MDR pressure and microbiota disruption; not recommended for low-intensity/palliative care. Posaconazole is advised for intensive chemotherapy with or without FLT3 inhibitors, venetoclax-based regimens, HMA with or without ivosidenib (first 4 cycles), but not APL/palliative care. Antiviral prophylaxis is recommended for APL receiving arsenic trioxide; limited evidence elsewhere. The panel supports universal pneumococcal, influenza, SARS-CoV-2 and herpes zoster vaccination. Overall, these consensus statements aim to harmonize practice and highlight key areas requiring specifically designed prospective studies.

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1. Introduction

Infections represent a major cause of morbidity and mortality in patients suffering from acute myeloid leukemia (AML), including acute promyelocytic leukemia (APL). These complications, driven by cytotoxic chemotherapy and subsequent severe or prolonged neutropenia, directly jeopardize survival, treatment continuity, clinical outcomes, and quality of life [1–4]. Antimicrobial prophylaxis as well as vaccinations play a crucial role in the management of patients with AML/APL by reducing the incidence of several infections and various scientific societies have issued guidelines on infection prevention strategies in this population based on literature analysis and expert opinion. (Table 1) [5–19]. Notably, international guidelines primarily focus on patients receiving intensive induction chemotherapy, frequently failing to provide specific recommendations for antibacterial (ABP), antifungal (AFP), antiviral (AVP), and vaccine prophylaxis across the full spectrum of AML/APL patients treated with lower-intensity regimens. Furthermore, many recommendations rely on historical data that may not reflect the evolving epidemiology of infections or modern leukemia management. Specifically, the routine use of fluoroquinolones (FQ) for ABP is currently being re-evaluated due to the rise of multi-drug-resistant (MDR) pathogens and the risk of persistent, disabling, and potentially irreversible adverse effects, as cautioned by American and European regulatory agencies [20,21]. Recent consensus literature studies clearly showed an increase of antimicrobial resistance in patients with hematological malignancies in Europe, highlighting the rationale for revisiting antibacterial prophylaxis strategies [22,23]. Consequently, infection prevention strategies vary significantly across hematology centers. To characterize this heterogeneity, a preliminary survey was conducted in May 2024 among 46 institutions within the GIMEMA (Gruppo Italiano Malattie EMatologiche dell'Adulto) cooperative group. The survey revealed marked inconsistencies in prophylaxis prescribing patterns across different leukemia settings, particularly regarding ABP post-intensive chemotherapy, AFP during less-intensive treatments, and the general application of AVP and vaccinations. Notably, ABP prescription rates ranged from 26% to 43% depending on the patient subset, findings consistent with recent international data reporting a 48% ABP utilization rate in Europe [24]. A more detailed description of this survey has been reported in supplementary material (Appendix A). To address these unmet clinical needs and bridge the gap between guidelines and real-world practice, a panel of experts from the GIMEMA AML and Infection Working Parties convened to analyze these critical issues, the results of which are synthesized in the current consensus project.

2. Methods

A leadership committee comprising three chairs (FM, CG, LP) appointed an expert panel of fourteen members, including eleven hematologists (FM, CG, AB, AC, CC, LF, MD, MIDP, NSF, AV, LP) and three infectious disease specialists (GG, EMT, MT), selected for their expertise in managing infections in AML/APL patients. Two additional experts in hematological clinical trial management (AP, MV) supported the project but did not participate in the formal consensus process. A consensus-based project applies the methodology of group discussion (questionnaires and nominal group technique). This means that the statements, advice, and recommendations generated may not primarily be evidence-based (they may not derive from a systematic review and grading of the evidence) because of the limited number of recent interventional, clinical studies dealing with prevention of infections in AML populations.

The panel conducted a preliminary survey of infection control strategies across Italian GIMEMA member centers (Appendix A). This surveillance focused on antimicrobial prophylaxis and vaccination across five distinct AML/APL clinical settings: a) AML undergoing intensive chemotherapy; b) APL undergoing induction therapy; c) AML undergoing therapy with hypomethylating agents in association with venetoclax; d) AML undergoing less intensive treatments; e) AML submitted to only supportive/palliative care. The survey results provided a framework for identifying the variability, uncertainties, and inconsistencies in current Italian clinical practice. Consequently, this project aimed to re-evaluate the indications for ABP, AFP, AVP, and vaccine prophylaxis, stratified by the treatment settings. During the initial meeting, the panel defined the project's scope and structural framework. The panel identified six clinical outcomes (Table 2) to evaluate the indications for or against anti-infective prophylaxis. Members conducted a comprehensive PubMed search of English-language literature (January 2012 to December 2025) focusing on infection epidemiology and prophylaxis strategies in AML patients using the terms “acute myeloid leukemia”, “acute promyelocytic leukemia”, “infections”, “epidemiology of infections”, “antifungal prophylaxis”, “antibacterial prophylaxis”, “antiviral prophylaxis” and “vaccination” for the search. The literature review work was divided into groups each of two or more experts based on the type of prophylaxis. Prospective and retrospective series with information relating to at least one of the above clinical otcomes were considered. Following a modified Delphi process, the experts formulated recommendations based on literature evidence, clinical relevance, and professional experience. We should highlight here that few of the recommendations have been additionaly based on the Italian law context, and, as a consequence may vary in other jurisdictions. An initial set of statements was drafted by a lead panelist; subsequently, the remaining members scored their level of agreement and proposed revisions. The process culminated in a final consensus meeting where participants discussed any remaining disagreements in a round-robin format before casting final votes. At least 70% consensus on the statement should have been obtained, otherwise the choices were discussed again and a second vote taken. If a 70% consensus was still not attained, no further attempt was made declaring the issue undecidable. This consensus work started from the premise that there are no recent controlled studies on the topic on which to base new guidelines with gradation of recommendations. Essentially, the consensus work focused on a binary Y/N outcome for each expert with whom the level of agreement (LoA) was defined.

3. Results

An extensive review of the scientific literature published from January 2012 to December 2025 has been carried out across the different settings of AML/APL by treatment strategy. All the studies addressing infections and antimicrobial prophylaxis, whenever available, have been resumed in supplementary tables, from table S1 to table S11.

3.1. Antibacterial prophylaxis in the different AML/APL settings

In patients at high risk of severe and prolonged neutropenia, the use of FQ-based ABP may still represent a reasonable strategy. Nevertheless, its application should be carefully selected and driven by local patterns of antimicrobial resistance. Although the recent guidelines continue to recommend ABP in patients with AML [1–3,7,14], such recommendations largely rely on earlier randomized clinical trials and meta-analyses, which showed a reduction in episodes of febrile neutropenia and microbiologically documented bacterial infections, while demonstrating a more limited and inconsistent effect on overall mortality [25,26]. However, the current clinical scenario is increasingly influenced by the emergence of resistance to FQ and, more broadly, by the global MDR organisms. Several recent observational studies, together with surveillance data, have reported a growing prevalence of FQ-resistant Gram-negative bacteria, particularly among Enterobacterales, in hematologic malignancy patients [22,23]. This trend may reduce the effectiveness of prophylactic strategies. Moreover, prior exposure to FQ has been associated with an increased risk of bloodstream infections caused by MDR Gram-negative pathogens [27,28]. In parallel, accumulating evidence suggests that FQ use can profoundly modify the intestinal microbiota in

Table 1
Main guidelines/recommendations regarding antimicrobial prophylaxis in AML/APL.

Antifungal prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/comments**
Pagano et al. Leukemia 2025	2025	ECIL	Adults	Clinical practice guidelines	*Standard induction chemotherapy* • PCZ 200 mg 300 mg tablets q24h (AI) • L-Amb 10 mg × 2 weekly nebulized (BI) • Fluconazole 400 mg q24h (BI) • Isavuconazole 200 mg q28h p.p first 2 days then 200 mg q24h (BIIt) • VCZ 6 mg/Kg/12 h first day then 4 mg/kg q12h i.v./p.o. (BIIu) • Micafungin 50 mg q24h i.v. (BIIu,t) • Caspofungin 50 mg q24h i.v. (70 mg on day 1, 70 mg q24h in patients >80 Kg *During neutropenic phases* • PCZ (category 1) • VCZ, Isavuconazole, Echinocandins, L-Amb or Fluconazole (category 2B) *Standard induction chemotherapy* • PCZ 200 mg TID suspension or 300 mg tablets qd (AI) • L-Amb 12.5 mg × 2 weekly nebulized (BII) • Isavuconazole 200 mg q24h i.v. q8h on days 1–2 (BIIt) • VCZ 4 mg/kg q12h i.v./p.o. (BIIu) • Micafungin 50 mg q24h i.v. (BIIu,t) *New induction regimens*
Baden et al. J Natl Compr Cancer Netw 2024	2024	NCCN	Adults	Guidelines	
Stemler et al. J Antimicrob Chem 2023	2022	AGIHO-DGHO	Adults	Recommendations	• Triazole prophylaxis in patients receiving Venetoclax with dose adjustment (AIIu,t) • Triazole prophylaxis in patients receiving Gilteritinib without dose adjustment (AIIu,t) • If indicated, triazole prophylaxis in patients receiving Midostaurin without dose adjustment (AIIu,t) • If indicated, triazole prophylaxis in patients receiving Quizartinib with dose adjustment if PCZ or VCZ (BIII) • If indicated, triazole prophylaxis in patients receiving Ivosidenib with dose adjustment if PCZ or VCZ (BIII) *New induction regimens*
Maschmeyer et al. Leukemia 2022	2022	ECIL	Adults	Clinical practice recommendations	• Standard of care in AML when GO is given in combination with chemo (AIIr) or high-dose GO for relapse (AIIr)(*) • No systemic prophylaxis for GO when given as monotherapy (AIIr) • No systemic prophylaxis for IDH1 or IDH2 inhibitors when given as monotherapy (AIIr) • No systemic prophylaxis for Gilteritinib when given as monotherapy (AIIr) • Standard of care in AML, when Midostaurin is given in combination with cytarabin/anthracycline chemo (AIIr) • No systemic prophylaxis for Midostaurin when given as monotherapy (AIIr) • Standard of care in AML when Quizartinib is given in combination with chemo (AIIr) • Standard of care in AML when Glasdegib is given in combination with chemo (AIIr) • Standard of care in AML when Venetoclax is given in combination with intensive chemo (AIIr) • Consider antifungal prophylaxis when hypomethylating agents are combined with Venetoclax (AIIr) • In PCZ is given in combination with Venetoclax reduce Venetoclax dose by 75% (AI) *New induction regimens*
Stemler et al. Lancet Haematol 2022	2022	EHA	Adults	Expert consensus recommendations	• Azacitidine conditional for antifungal prophylaxis. Not generally recommended, but should be considered in patients pretreated with chemotherapy, in those with neutropenia at treatment initiation, or those with previous IFD

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Table 1 (*continued*)

Antifungal prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/comments**
					• Decitabine conditional for antifungal prophylaxis. Not generally recommended, but should be considered in patients pretreated with chemotherapy, in those with neutropenia at treatment initiation, or those with previous IFD • Venetoclax conditional for antifungal prophylaxis. Preferably with a triazole; adapt dose when using PCZ or VCZ concomitantly • Midostaurin strong recommendation for triazoles during remission-induction treatment. Closely monitor for DDI • In Gilteritinib monotherapy, no benefit of antifungal prophylaxis; triazole prophylaxis should be considered in patients pretreated with chemotherapy or patients with long lasting neutropenia • Quizartinib: strong recommendation for triazoles during remission-induction treatment, with a dose reduction of Quizartinib; in monotherapy, no recommendation for antifungal prophylaxis • Sorafenib: strong recommendation for triazoles during remission-induction treatment • GO: strong recommendation for triazoles during remission-induction treatment • Glasdegib, Enasidenib and Ivosidenib: only consensus statements *Standard induction or re-induction chemotherapy* Adults
The et al. Int Med J 2021	2021	Australasian Antifungal Guidelines Steering Committee	Adults and children	Consensus guidelines	• PCZ loading dose 300 mg twice daily on day 1 followed by 300 mg daily (AI) • VCZ 4 mg/Kg daily i.v./p.o. (AII) • Micafungin 100–150 mg daily (BII) • Itraconazole 200 mg twice daily (BII) • L-Amb 50–200 mg three times per week (BII) Children ▪ Routine mold-active prophylaxis is recommended (AI) *Standard chemotherapy*
Lehrnbecher et al. J Clin Oncol 2020	2020	Expert panel supported by the Pediatric Group of Ontario	Children	Clinical practice guidelines	• Systemic antifungal prophylaxis to children and adolescents receiving AML treatment that is expected to result in profound and prolonged neutropenia (strong recommendation, high-quality evidence) • Administer a mold-active agent (strong recommendation, high-quality evidence) • Echinocandin or a mold-active azole (strong recommendation, moderate-quality evidence) *Standard induction chemotherapy*
Maertens et al. J Antimicrob Chem 2018	2018	ECIL	Adults	Guidelines	• PCZ 200 mg TID suspension or 300 mg tablets qd (AI) • Fluconazole 400 mg q24h (BI) • Itraconazole oral solution 2.5 mg/Kg q12h (BI) • VCZ 200 mg q12 (BII) • Aerosolized L-Amb 10 mg twice weekly only combined with systemic Fluconazole (BI) *Re-induction or intensified consolidation therapy*
Taplitz et al. J Clin Oncol 2018	2018	ASCO-IDSA	Adults	Clinical practice guidelines	• Primary antifungal prophylaxis may be considered in this setting (no grade) *Standard chemotherapy* • Antifungal prophylaxis with an oral triazole or parental echinocandin is recommended (moderate recommendation, intermediate-quality evidence) • Antifungal prophylaxis should be given during period od expected neutropenia (moderate recommendation, intermediate-quality evidence) *Standard induction chemotherapy* Adults
Ullman et al. Clin Microb Infect 2018	2017	ESCMID-ECMM-ERS	Adults and children	Guidelines	

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Table 1 (*continued*)

Antifungal prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/comments**
					• PCZ 200 mg TID suspension or 300 mg tablets qd (AI) • L-Amb 12.5 mg × 2 weekly nebulized in association to systemic Fluconazole (BI) Children
					• Itraconazole (A/B IIt) • PCZ, VCZ (AIIt) • L-Amb, Micafungin (B IIt/III) *Standard induction and consolidation chemotherapy*
Baden et al. J Natl Compr Canc Netw 2016	2016 (updated version 2.2023)	NCCN	Adults	Guidelines	• PCZ (category 1) • VCZ, Isavuconazole, Echinocandins, L-Amb or Fluconazole (category 2B) *Standard induction or re-induction chemotherapy*
Groll et al. J Lancet Oncol 2014	2014	ECIL	Children	Guidelines	• Fluconazole 8–12 mg/Kg (max 400 mg) q24h i.v./p.o. (AIIt) • Patients aged 13 years or older: delayed-release tablets, 300 mg in one single daily dose (2 × 300 mg on day 1); patients aged 1 month to 12 years: oral suspension, starting dose 6 mg/kg three times daily (AIIt) • Patients aged 2 years or older: 5 mg/kg per day orally in two divided doses (BIIt) • L-Amb 1 mg/kg every other day i.v. (BIIt) • L-Amb 2.5 mg/kg twice per week i.v. (BII) • VCZ. Patients aged 2–12 years, or aged 12–14 years and weighing less than 50 kg: 8 mg/kg (9 mg/kg on day 1) twice a day i.v. or 9 mg/kg twice a day p.o. Patients aged 12–14 years and weighing 50 kg or more, or aged 15 years and older: 4 mg/kg (6 mg/kg on day 1) twice a day i.v. or 200 mg twice a day p.o. (BIIt)
Antibacterial prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/Comments**
					Standard induction and consolidation chemotherapy
Baden et al. J Natl Compr Cancer Netw 2024	2024	NCCN	Adults	Guidelines	• Consider fluoroquinolones prophylaxis during neutropenia *New induction regimens*
Maschmeyer et al. Leukemia 2022	2022	ECIL	Adults	Clinical practice recommendations	• Standard of care in AML when GO is given in combination with chemo (AIIr) or high-dose GO for relapse (AIIr)(*) • No systemic prophylaxis for GO when given as monotherapy (AIIr) • No systemic prophylaxis for IDH1 or IDH2 inhibitors when given as monotherapy (AIIr) • No systemic prophylaxis for Gilteritinib when given as monotherapy (AIIr) • Standard of care in AML, when Midostaurin is given in combination with cytarabin/anthracycline chemo (AIIr) • No systemic prophylaxis for Midostaurin when given as monotherapy (AIIr) • Standard of care in AML when Quizartinib is given in combination with chemo (AIIr) • Standard of care in AML when Glasdegib is given in combination with chemo (AIIr) • Standard of care in AML when Venetoclax is given in combination with intensive chemo (AIIr) • Consider antibacterial prophylaxis when hypomethylating agents are combined with Venetoclax (AIIr) • Ensure proper Venetoclax dose adjustment when combined with ciprofloxacin or macrolides (AI) *Standard chemotherapy in newly diagnosed or relapsed AML*
Lehrnbecher et al. Lancet Oncol 2021	2020	ECIL	Children	Guidelines	• The ECIL-8 group does not recommend routine antibacterial prophylaxis for pediatric patients (DIII)

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Table 1 (*continued*)

Antifungal prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/comments**
					Standard chemotherapy
Taplitz et al. J Clin Oncol 2018	2018	ASCO-IDSA	Adults	Clinical practice guidelines	• Antibacterial prophylaxis with fluoroquinolones is recommended in patients at high-risk of febrile neutropenia or profound and protracted neutropenia (moderate recommendation, high-quality evidence) • Antibacterial prophylaxis with fluoroquinolones should be given during period od expected neutropenia (moderate recommendation, high-quality evidence)
					Standard induction chemotherapy
Mikulska et al. J Infect 2018	2018	ECIL	Adults	Critical appraisal of previous guidelines	• No data have been found contradicting the ECIL-1 recommendation in favor of fluoroquinolones prophylaxis in AML patients with profound and prolonged neutropenia in order to prevent infections (not impact on survival) • Local antibiotic policies on fluoroquinolones prophylaxis use should be in line with national antimicrobial stewardship programs and based on local epidemiological data
					Standard induction and consolidation chemotherapy
Baden et al. J Natl Compr Canc Netw 2016	2016 (updated version 2.2023)	NCCN	Adults	Guidelines	• Consider fluoroquinolones prophylaxis during neutropenia in AML patients (category 2 A)
Antiviral prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/Comments**
					Neutropenic phases
Baden et al. J Natl Compr Cancer Netw 2024	2024	NCCN	Adults	Guidelines	• HSV prophylaxis (**) during active therapy including periods of neutropenia • Antiviral prophylaxis is not routinely required during intensive leukemia treatment for preventing VZV • During remission induction chemotherapy Acyclovir or Valacyclovir should be administered to prevent HSV stomatitis and other clinical manifestations of HSV (BIIr) • Antiviral prophylaxis with a nucleoside analog (eg, acyclovir) is recommended in HSV-seropositive patients undergoing leukemia induction therapy until recovery of the WBC count or resolution of mucositis, whichever occurs later; duration can be extended for people with frequent recurrent HSV infections
Girmenia et al. Haematologica 2024	2024	"ad hoc" Italian expert panel	Adults	Position paper	
Henze et al. Ann Hematol 2022	2022	AGIHO-DGHO	Adults	Guidelines	
Taplitz et al. J Clin Oncol 2018	2018	ASCO-IDSA	Adults	Clinical practice guidelines	
					Active chemotherapy Adults
Baden et al. J Natl Compr Canc Netw 2016	2016 (updated version 2.2023)	NCCN	Adults and children	Guidelines	• HSV prophylaxis is indicated during active therapy including period of neutropenia (category 2 A) Children • HSV prophylaxis is indicated in seropositive patients (category 2 A) • VZV prophylaxis is not routinely indicated unless there is a history of recurrent zoster infections or after 1st zoster episode while on myelosuppressive therapy, even if they are seropositive or vaccinated (category 2 A)
Vaccinations					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/Comments**
Von Lilienfeld-Toal et al. Lancet Infect Dis 2026	2025	ECIL	Adults and children	Recommendations	• Annual seasonal influenza vaccine administration is recommended at the beginning of the influenza season to all adults and pediatric patients. Vaccination should be repeated annually (AIIt) • Passive immunization for RSV should not be used for RSV pre-exposure or post-exposure prophylaxis (DII) • Seasonal pre-exposure prophylaxis with palivizumab could be considered for children <2 years when a nosocomial outbreak is occurring (BIII)
Cesaro et al. Leukemia 2025	2025	ECIL	Adults	Recommendations	• Patients with hematologic malignancies who were never vaccinated should receive a primary vaccination program

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Table 1 (*continued*)

Antifungal prophylaxis					
Reference	**Year**	**Society**	**Population**	**Type of paper**	**Evidences/comments**
Baden et al. J Natl Compr Cancer Netw 2024	2024	NCCN	Adults	Guidelines	against SARS-CoV-2 according to international and national authorities (AIIu) • Patients with hematologic malignancies who were vaccinated with a full vaccination program should receive at least yearly booster doses with an updated vaccine against SARS-Cov_2 according to country recommendations (AIIu) • Inactivated or recombinant influenza vaccine: all patients, annually • SARS-CoV-2: all cancer patients • Pneumococcal vaccines: pneumococcal conjugate vaccine (PCV20) should be administered to adult patients who are newly diagnosed with cancer • Recombinant VZV vaccine is recommended for adult patients 50 years-old or older and those 18 years old or older who are at increased risk of VZV, given in two doses 2–6 months apart
Girmenia et al. Haematologica 2024	2024	"ad hoc" Italian expert panel	Adults	Position paper	• Recombinant VZV vaccine should be considered after leukemia treatment discontinuation, particularly in elderly patients • Inactivated influenza vaccine: at the end of intensive chemotherapy, a single dose is recommended yearly if the patient is considered immunocompromised (BIIu) • Pneumococcal vaccines: 3–6 months after the end of chemotherapy, patients should be (re) vaccinated according to age and country recommendations
Mikulska et al. Lancet Infect Dis 2019	2017	ECIL	Adults	Guidelines	• HBV vaccination: in countries with high HBV prevalence where a high risk of HBV transmission during chemotherapy exists, HBV vaccination starting before and continuing during chemotherapy can be administered (CIIu) • Other inactivated vaccines: 3–6 months after the end of chemotherapy, should be (re) vaccinated according to age and country recommendations

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia; ECIL: European Conference on Infections in Leukemia; PCZ: posaconazole; VCZ: voriconazole; L-Amb: Liposomal amphotericin B; AGIHO-DGHO: Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology; GO: Gemtuzumab ozogamicin; EHA: European Hematology Association; IFD: invasive fungal disease; ASCO: American Society of Clinical Oncology; IDSA: Infectious Diseseases Society of America; ESCMID: European Society of Clinical Microbiology and Infectious Diseases; ECMM: European Confederation of Medical Mycology; ERS: European Respiratory Society; NCCN: National Comprehensive Cancer Network; VZV: varicella-zoster virus; HSV: herpes simplex virus; RSV: respiratory syncytial virus; HBV: hepatitis B virus.
(*) Standard of care means PCZ and fluoroquinolones for antifungal and antibacterial prophylaxis, respectively.
(**) Oral acyclovir 400 to 800 mg/day, oral valaciclovir 500 mg BID or oral famciclovir 250 mg BID.

patients with hematological malignancies. Such alterations may compromise colonization resistance, thereby facilitating the expansion of MDR organisms, with potential life-threatening consequences [29,30]. Within this evolving framework, strategies based on risk stratification and ecological considerations appear more appropriate than a universal prophylactic approach.

Intensive chemotherapy (7 + 3 and liposomal daunorubicin and cytarabine, CPX-351) Overall, from all the studies analysed [31–41], ABP does not affect overall survival (OS) but impacts in decreasing febrile and infectious episodes in patients receiving conventional 7 + 3 induction. Indeed, there are some data suggesting a negative impact on selective pressure of multi-drug-resistant strains [28,42] and on adverse effects, particularly in terms of negative pressure on microbiota balance [29,30]. No sufficient data have been published on the impact of ABP in the leukemia treatment schedule and quality of life. Detailed data have been summarized in Table S1. Specific data for patients treated with CPX-351 are lacking [43–58]; nevertheless, the panel suggests that findings from conventional 7 + 3 induction may be extrapolated to this cohort. Detailed data have been summarized in Table S2.

Gemtuzumab Ozogamicin (GO)-based or Fludarabine-based intensive chemotherapy. Overall, from all the studies analysed [59–73], no sufficient data have been published about the clinical outcomes selected by the panel specifically related to GO-based or fludarabine-based intensive chemotherapy for ABP. However, most of the information might be translated from that reported for other intensive chemotherapy treatment schedules (i.e. 7 + 3). Detailed data have been summarized in Table S3 and Table S4.

Intensive chemotherapy plus FLT3 inhibitors. No specific data have been

Table 2
Clinical outcomes of infections prevention in adult AML/APL populations.

Clinical outcomes
To prevent a life-threatening infection
To prevent an infection (including fever of unknown origin), representing a potential risk for prolonged hospitalization (in inpatients) or rehospitalization (in outpatients).
To prevent an infection that may impact on patient's quality of life.
To prevent an infection that may interfere with the leukemia treatment schedule.
Contraindication due to side effects
Contraindication due to significant impact on the emergence of antimicrobial resistance.

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia.

published about the clinical outcomes selected by the panel for ABP in patients AML treated with intensive chemotherapy plus FLT3 inhibitors [74–91]. However, most of the information might be translated from that reported for conventional 7 + 3 induction. Detailed data have been summarized in Table S5.

APL patients treated with chemo-based or ATO-based regimens. No specific data have been published about the clinical outcomes selected by the panel specifically related to this setting of patients [92–113]. We only know from scientific literature that ABP can negatively affect adverse effects in APL patients, since it is known that FQ may impact the QTc interval [114], potentially delaying ATO administration which is crucial in terms of survival outcomes. Detailed data have been summarized in Table S6.

Hypomethylating agents (HMA) in association with venetoclax. Overall, from all these published data [115–120], ABP significantly reduces the risk of infectious episodes, which are most frequent during the first two cycles of therapy when neutropenia and active leukemia coexist. However, no sufficient data have been published on the impact of ABP among the other clinical outcomes selected by the panel for this regimen. Detailed data have been summarized in Table S7.

Less intensive regimens (HMA alone, HMA + ivosidenib, low dose cytarabine + glasdegib). Overall, no specific data has been published about the clinical outcomes selected by the panel specifically related to therapy with other less intensive regimens (HMA alone, HMA + ivosidenib, low dose cytarabine + glasdegib) for ABP [121–142]. Detailed data have been summarized in Table S8.

Patients submitted to only supportive/palliative care. No specific data has been published about the clinical outcomes selected by the panel specifically related to patients submitted to only supportive/palliative care for ABP [115–136]. Detailed data have been summarized in Table S8.

PANEL RECOMMENDATION (Table 3). As shown in Table 3, the level of agreement of the panel on this topic is low (28%). FQ-based ABP still decreases infectious episodes, including bacteremia by susceptible gram-negative strains, but a significant effect on OS has never been demonstrated. The choice of whether or not to use FQ-based ABP depends on various factors that can locally affect the outcome of gram-negative infections, including the possibility of early empirical antibiotic therapy. In addition, these data have been obtained almost 20 years ago, with a completely different epidemiologic scenario. If we consider the current and progressive increase in multi-drug-resistant strains, widely documented in the overall population by the annual epidemiologic reports of the European Centre for Disease Prevention and Control (ECDC) [143], ABP should be carefully evaluated to avoid negative impact on selective pressure. Moreover, ABP might be related to a detrimental effect on patient microbiota. Finally, different types of serious adverse events have been associated with FQ use in the general population, so that several warnings on their use have been so far published by the main international agencies. Same considerations for patients receiving venetoclax-based regimens. As for patients treated with less intensive regimes (i.e. HMA alone or HMA + Ivosidenib or LDAC + Glasdegib) or AML patients submitted to only supportive/palliative care, the panel agrees that ABP is not generally recommended.

Table 3
Recommendations on the use of antibacterial prophylaxis (ABP) in the different AML/APL settings.

AML setting	Recommendations	LoA
AML non-APL undergoing intensive chemotherapy, including combinations with FLT3 inhibitors and GO	ABP with FQ is recommended during neutropenia after induction intensive chemotherapy.	28%
APL undergoing induction therapy	ABP with FQ is recommended during neutropenia after chemo-based induction intensive chemotherapy and in patients receiving ATO-based induction regimens in case of prolonged and severe neutropenia or concomitant risk factors (i.e. smoking, advanced age, COPD).	28%
AML undergoing therapy with HMA agents in association with venetoclax	ABP with FQ is recommended particularly during the first 2 cycles of treatment.	28%
AML undergoing less intensive treatments (HMA alone or HMA + Ivosidenib or LDAC + Glasdegib)	Literature data show a moderate risk of bacterial infections particularly during the first cycles of treatment. ABP in this AML population is not generally recommended.	85%
AML submitted to only supportive/palliative care	There is not extensive literature on bacterial infections in patients ineligible for any treatment undergoing best supportive care/ palliative care. ABP with FQ is not recommended.	100%

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia; LoA: level of agreement; GO: Gemtuzumab ozogamicin; ABP: antibacterial prophylaxis; FQ: fluoroquinolones; ATO: arsenic trioxide; HMA: hypomethylating agents; LDAC: low-dose cytarabine; COPD: chronic obstructive pulmonary disease.

3.2. Antifungal prophylaxis in the different AML/APL settings

Recent guidelines address in detail the issue of AFP in AML patients treated with intensive chemotherapy or less intensive regimens [1–3,5–13]. However, they still do not completely cover some emergent issues, such as elderly patients treated with new less intensive regimens (i.e. HMA + Ivosidenib, LDAC + Glasdegib, oral decitabine) or AML patients submitted to only supportive care/palliative care. In addition, data about invasive fungal disease (IFD) during the consolidation phases are scarce and AFP role in those phases is still under debate.

Intensive chemotherapy (7 + 3 and CPX-351) Overall, from all the studies analysed [28–58], AFP is significantly associated with improved survival, reduces IFD and complications interfering with the leukemia treatment schedule in patients treated with conventional 7 + 3. In addition, AFP is not associated with significant adverse effects and there is not clear evidence that AFP may determine a selective pressure leading to resistant fungal strains in AML in-patient population. Detailed data have been summarized in Table S1. As for patients receiving CPX-351, AFP significantly affects survival and leukemia treatment schedule (Table S2). In constrast to that observed in the induction phases, evidence for AFP during AML consolidation remains limited. Although IFD is relatively rare in this phase, it is associated with high mortality in patients over 60 [144]. AFP with mold-active agents (e.g., posaconazole) should be considered in higher-risk settings, such as older patients or those receiving high-dose cytarabine or other intensive regimens.

Gemtuzumab Ozogamicin (GO)-based or Fludarabine-based intensive chemotherapy. No sufficient data have been published about the clinical outcomes selected by the panel specifically related to GO-based or fludarabine-based intensive chemotherapy for AFP [59–73]. However, most of the information might be translated from that reported for other intensive chemotherapy treatment schedules (i.e. 7 + 3). Detailed data have been summarized in Table S3 and Table S4.

Intensive chemotherapy plus FLT3 inhibitors. AFP significantly affects survival and IFD episodes, leukemia schedule and quality of life in AML patients receiving intensive chemotherapy plus FLT3 inhibitors. AFP may lead to an increase in adverse effects, particularly related to drug-drug interactions with FLT3 inhibitors (i.e. QTc prolongation, hepatotoxicity). Therefore, caution and careful monitoring for cardiac toxicity should be used, particularly in older patients [88]. There is not clear evidence that might be responsible for the increase of resistant fungal infections in AML in-patient population [74–91]. Detailed data have been summarized in Table S5.

APL patients treated with chemo-based or ATO-based regimens. From all the studies analysed, an overall low risk of IFD in this setting has been reported, regardless of treatment schedule, both chemo-free and chemo-

based [92–113]. Only few specific studies have been published about the clinical outcomes selected by the panel specifically related to AFP in this setting of patients [106,109]. Analysed studies have been summarized in Table S6.

HMA in association with venetoclax. AFP significantly reduces the risk of infectious episodes in this setting of patients and is not associated with significant adverse effects. No sufficient data has been published on its impact among the other clinical outcomes selected by the panel [115–120]. Detailed data on analysed studies have been summarized in Table S7.

Less intensive regimens (HMA alone, HMA + ivosidenib, low dose cytarabine + glasdegib). Literature data show a moderate risk of invasive fungal infections particularly during the first cycles of treatment [122,124,131–133,138,140,145–150]. However, no specific data has been published about the clinical outcomes selected by the panel specifically related to this setting of patients for AFP. All the analysed studies data have been summarized in Table S9.

Patients submitted to only supportive/palliative care. No specific data has been published about the clinical outcomes selected by the panel specifically related to patients submitted to only supportive/palliative care for AFP [122,124,131–133,138,140,145–150]. All the analysed studies data have been summarized in Table S9.

PANEL RECOMMENDATION (Table 4). The recent guidelines recommended the use of AFP in AML patients treated with intensive chemotherapy [1–3,5–13]. The panel agrees to recommend AFP with posaconazole in this setting of patients, as shown in Table 4. In addition, AFP with posaconazole is recommended also for induction regimens containing FLT3 inhibitors and GO. However, in patients treated with FLT3 inhibitors caution and careful monitoring for cardiac toxicity should be used, particularly in older patients. As for APL patients, the panel agrees that AFP is not generally recommended, regardless of treatment schedule, and might be considered only in center with high rates of mold infections for APL patients submitted to chemo-based programs. AFP with posaconazole is generally recommended for AML patients receiving HMA agents in association with venetoclax, particularly in the first 4 cycles of treatment. Venetoclax dosage should be decreased by 75% (typically 100 mg) when co-administered with posaconazole. AFP with posaconazole is suggested in the first 4 cycles or until neutrophil recovery in patients treated with HMA alone. Although there is not specific information about patients receiving HMA plus ivosidenib, most of the information might be translated from that reported for patients treated with HMA alone. However, in patients who receive ivosidenib or glasdegib, drug-drug interactions (DDI) and possible QTc prolongation should be considered. Finally, there are not solid data to recommend AFP in AML patients submitted to only supportive/palliative care.

Table 4
Recommendations on the use of antifungal prophylaxis (AFP) in the different AML/APL settings.

AML setting	Recommendations	LoA
AML non-APL undergoing intensive chemotherapy, including combinations with FLT3 inhibitors and GO	AFP with posaconazole (preferably tablet formulation) is recommended until complete remission and/or neutrophils recovery. In patients treated with intensive chemotherapy + FLT3 inhibitors AFP is recommended but caution and careful monitoring for cardiac toxicity should be used, particularly in older patients.	100%
APL undergoing induction therapy	AFP is not generally recommended, due to the low risk of invasive fungal disease in this setting, regardless of treatment schedule. In centers with high rates of mold infections, AFP may be considered in chemo-based induction regimens with the goal of preventing infections that may interfere with the leukemia treatment schedule.	100%
AML undergoing therapy with HMA agents in association with venetoclax	AFP with posaconazole (preferably tablet formulation) is recommended in the first 4 cycles, starting at the end of the venetoclax ramp-up. Venetoclax dose should be reduced by 75% when posaconazole is concomitantly administered.	78%
AML undergoing less intensive treatments (HMA alone or HMA + Ivosidenib or LDAC + Glasdegib)	Literature data show a moderate risk of invasive fungal infections particularly during the first cycles of treatment. AFP with posaconazole (preferably tablet formulation) is suggested in the first 4 cycles or until neutrophils recovery. In patients who receive ivosidenib or glasdegib, DDI and possible QTc prolongation should be considered.	78%
AML submitted to only supportive/palliative care	There is not extensive literature on fungal infections in patients ineligible for any treatment undergoing best supportive care/ palliative care therefore AFP is not recommended.	100%

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia; LoA: level of agreement; GO: Gemtuzumab ozogamicin; AFP: antifungal prophylaxis; HMA: hypomethylating agents; LDAC: low-dose cytarabine; DDI: drug-drug interactions.

3.3. Antiviral prophylaxis in the different AML/APL settings

AVP against Herpes Simplex Virus (HSV) and Varicella-Zoster Virus (VZV) is recommended in AML/APL patients receiving intensive chemotherapy by many international guidelines [1–3,16]. However, only very few studies have been published addressing this issue in AML patients and the only randomized one has been published almost 30 years ago [151]. From all the studies analysed in our extensive review of the scientific literature published from January 2012 to December 2025, no specific data have been published about the clinical outcomes selected by the panel specifically related to the different AML settings. As for APL patients, a higher rate of viral recurrence in patients treated with the ATO-based approach is clear from the analysis of the scientific literature [102–104]. ATO usage was significantly associated with the development of VZV reactivation compared to those treated without ATO [113].

PANEL RECOMMENDATION (Table 5). Based on scarse evidence specifically coming out on AML patients from the scientific literature, the level of agreement of the panel about the recommendation on the use of AVP in AML patients treated with intensive chemotherapy is low (14%). On the contrary, the panel completely agrees that all APL patients receiving ATO-based regimens should receive AVP until 6 months after ATO discontinuation. Finally, the panel fully agrees that there is low evidence to support the use of AVP in all the other AML settings (i.e. HMA + venetoclax, HMA alone, HMA + Ivosidenib, LDAC + Glasdegib, supportive/palliative care).

3.4. Vaccinations in AML/APL patients

An extensive review of the scientific literature published from January 2012 to December 2025 has been carried out on anti-pneumococcal, anti-influenza, anti-SARS-CoV-2, anti-VZV and anti Respiratory Syncitial Virus (RSV) vaccinations in patients with AML/APL. We need to specify that we did not analyze data about AML patients undergoing allogeneic stem cell transplantation and that separate guidelines about vaccination strategies already exist for this specific subset.

Invasive pneumococcal disease. The risk of invasive pneumococcal disease (IPD) is increased among patients with hematologic malignancies. In a study population which included all individuals aged ≥15

Table 5
Recommendations on the use of antiviral prophylaxis (AVP) in the different AML/APL settings.

AML setting	Recommendations	LoA
AML non-APL undergoing intensive chemotherapy, including combinations with FLT3 inhibitors and GO	AVP (acyclovir, valacyclovir or famciclovir)* is recommended for 3–5 weeks after the start of chemotherapy.	14%
APL undergoing induction therapy	All patients receiving ATO-based regimens should receive AVP (acyclovir, valacyclovir), until 6 months after ATO discontinuation with the goal of preventing HZ infection and related complications.	100%
AML undergoing therapy with HMA agents in association with venetoclax	Literature data do not report frequent or severe HSV or VZV infections during HMA and venetoclax treatment therefore AVP is not recommended.	100%
AML undergoing less intensive treatments (HMA alone or HMA + Ivosidenib or LDAC + Glasdegib)	Literature data do not report frequent or severe HSV or VZV infections during HMA alone or combined with ivosidenib or LDAC + Glasdegib therefore AVP is not recommended.	100%
AML submitted to only supportive/palliative care	There is not extensive literature on viral infections in patients ineligible for any treatment undergoing best supportive care/palliative care therefore AVP is not recommended.	100%

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia; LoA: level of agreement; GO: Gemtuzumab ozogamicin; AVP: antiviral prophylaxis; HMA: hypomethylating agents; LDAC: low-dose cytarabine; ATO: arsenic trioxide; HSV: herpes simplex; VZV: varicella-zoster virus.

* we recommend using oral acyclovir 400 to 800 mg/day, oral valaciclovir 500 mg BID or oral famciclovir 250 mg BID.

years during 2000–2016 in Denmark the risk of IPD in patients with AML was 26 times higher when compared to the background population [152]. Few data are available specifically on pneumococcal vaccination in adult AML patients even though some data could be extrapolated from pediatric studies which demonstrate the efficacy of revaccination with a booster after the end of chemotherapy [19].

Influenza infection. Patients with cancer are at high risk for mortality and morbidity from seasonal influenza, with an estimated 20% to 30% of hospitalized patients with cancer testing positive for influenza and mortality rates as high as 10% during influenza seasons. However, there are no recent data on the risk of influenza infection specifically in patients with AML submitted to the current antileukemic treatments. In a population-based study from Ontario, Canada, vaccine effectiveness against laboratory-confirmed influenza was only 8% for patients with hematologic malignancies without details in the different hematologic diseases. The patterns of immune reconstitution following consolidation chemotherapy in AML patients in remission were explored in 10 patients using the response to seasonal influenza vaccination as a surrogate for the robustness of the immune system [153]. Only 2 of 10 patients generated protective titres in response to vaccination, and many patients had abnormal frequencies of transitional and memory B-cells, while, frequencies of T-cell populations were like those seen in healthy controls, and cytotoxic T-cells demonstrated antigen-specific activity after vaccination. These results suggest that while some aspects of cellular immunity recover quickly, humoral immunity is incompletely reconstituted in the year following intensive cytotoxic chemotherapy for AML. The observed B-cell abnormalities may explain the poor response to vaccination often seen in AML patients after chemotherapy. Although the seroconversion rates to one influenza vaccine dose is not higher than 20%, yearly vaccination is recommended out of intensive chemotherapy particularly in elderly patients [17,19,153,154]. Several strategies to improve immunogenicity of influenza vaccine have been described (i.e. high-dose vaccines, repetitive doses, ecc.), but we did not discuss here in detail about this topic.

SARS-CoV-2. The epidemiology and outcome of AML patients with SARS-CoV-2 was evaluated in a multicentre study of 388 AML/APL patients between February 2020 and October 2021 (pre-Omicron period) [155]. Many patients were receiving or had received AML treatment in the preceding 3 months. SARS-CoV-2 was severe in 41.2% and critical in 21.1% of cases. The chemotherapeutic schedule was delayed or discontinued in 44.8% of patients. After a median follow-up of 325 days, 46.4% of patients had died; death was attributed to SARS-CoV-2 (43.3%), AML (26.1%) or to a combination of both (26.7%). Another registry-based study with prospective data collection evaluated SARS-CoV-2 clinical severity and mortality in a population with hematologic malignancies including 148 adult AML patients diagnosed with SARS-CoV-2 between February 2020 and October 2022. This study was able to evaluate the epidemiology and clinical presentation of the infection during the Omicron compared to pre-Omicron period. Actuarial 30-day survival in hospitalized AML patients with SARS-CoV-2 in pre-Omicron and Omicron time periods was 89% and 59%, respectively [156]. In both periods SARS-CoV-2 vaccination was associated with greater survival rates. No study of SARS-CoV-2 vaccination has been focused on AML patients, however, an analysis of a subset of 126 patients with AML reported in 6 studies during the pre-Omicron period showed a seropositivity rate of 93% after 2 doses of SARS-CoV-2 vaccine [157]. Although few vaccination data of the Omicron period are available specifically in AML patients, to our opinion SARS-CoV-2 vaccination continues to represent a crucial tool in the infection-control strategy of SARS-CoV-2 in AML adult patients. It should be emphasized, however, that recent epidemiological data show that the spread and pathogenicity of the circulating SARS-CoV-2 variants have decreased. Vaccination recommendations may likely be revised in the near future; however, we do not believe it appropriate to reduce our level of vigilance and prevention strategies at this time until clear evidence of a favorable epidemiological trend emerges.

Herpes zoster (HZ). The risk of HZ infection is 2–3 times higher in AML patients compared to a non-cancer patient population [158,159]. It varies according to age of the patient and type of treatment. Data on incidence of HZ infection specifically in myeloid disorders were derived from three retrospective observational studies in APL [102–104,113]. APL patients treated with arsenic trioxide are at high risk of HZ if not receiving AVP; indeed, the incidence ranges from 11.6% to 45.7% within the first 6 months of therapy. The risk is particularly high for older patients and for those with a previous history of HZ. AVP was shown to significantly reduce the risk of HZ or delay its onset [102–104]. As far as we know about the protective effect of adjuvated recombinant HZ vaccine, Dagnew et al. [160] reported 80.4% and 73.7% of humoral and cellular vaccine response, respectively, in an adult immunocompromised population, including patients with AML and MDS (56 patients in the vaccine group).

Respiratory Syncitial Virus (RSV). RSV is a highly contagious virus and a leading global cause of acute lower respiratory tract infections. It primarily infects infants and young children but it also causes a significant burden of severe disease and mortality in older adults and individuals with underlying medical conditions including cancer, including hematologic malignancies [161,162]. Active immunization against RSV is currently licensed for adults older than 60 years and those at risk for severe low respiratory tract infections. Recent ECIL guidelines have no recommendation on RSV vaccination considering also that vaccine effectiveness efficacy and safety in patient populations with hematological malignancies or undergoing allogeneic stem cell transplant have not been defined [17]. However, recent guidelines from the German Society of Hematology and Medical Oncology Infectious Disease Working Group (AGIHO) recommended RSV vaccine administration in AML patients to prevent severe RSV illness with a BII grade of recommendation [163].

PANEL RECOMMENDATION (Table 6). Based on all analysed published studies, the panel fully agrees that anti-pneumococcal vaccination

with 20-valent pneumococcal conjugate vaccine (PCV-20) and seasonal (once a year) anti-influenza vaccination are recommended in all AML/APL patients particularly in older patients (≥ 65 years). It should be administered preferentially before starting antileukemic therapy. If delivery of vaccination is not feasible before therapy start, it can be administered at any time in less intensive treatments and after treatment discontinuation in patients submitted to intensive chemotherapy. The panel agrees that anti-SARS-CoV-2 (at least once a year) and anti-VZV vaccination with adjuvated recombinant HZ vaccine are generally suggested in AML/APL patients, preferentially before starting antileukemic therapy, particularly in older patients (≥ 65 years). RSV vaccination in AML patients may be considered preferably before treatment or after intensive chemotherapy discontinuation.

3.5. Prophylaxis of hepatitis B virus (HBV) reactivation in AML/APL patients

From the extensive review of scientific literature published from January 2012 to December 2025, we found a single published study specifically focused on AML patients, suggesting a significant decrease of HBV reactivation among HBV carriers patients receiving prophylaxis with anti-HBV agents [164]. However, the management of HBV reactivation in AML/APL patients receiving cytotoxic chemotherapy is quite similar to that reported for hematologic malignancies at high risk of HBV reactivation such as patients undergoing B-cell depleting agents or hematopoietic stem cell transplantation [3,165–171]. The goal of HBV prophylaxis is to prevent HBV reactivation and liver disease that could be a life-threatening complication that may also interfere with the leukemia treatment schedule.

PANEL RECOMMENDATION (Table 7). The panel fully agrees that the use of third-generation antiviral drugs (entecavir, tenofovir or tenofovir alafenamide) is recommended in HBsAg-positive AML/APL patients regardless of HBV DNA levels. Antiviral prophylaxis should be initiated at least 1 week before or in concomitance with starting cytotoxic chemotherapy. It should be continued for the duration of cytotoxic chemotherapy and administered for at least 12 to 24 months after chemotherapy withdrawal. Patients receiving cytotoxic chemotherapy with resolved HBV infection (HBcAb positive, HBsAg negative, HBV DNA negative) should receive antiviral prophylaxis. In recent years international guidelines [3,168–170] have proposed the use of third-generation antiviral drugs (entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide), rather than lamivudine, in patients at low risk of HBV reactivation, such as those who are HBsAg-negative/HBcAb-positive and HBV DNA negative undergoing cytotoxic chemotherapy due to resistance profile. In contrast, recent Italian guidelines [167] again recommend the use of lamivudine in hematological HBsAg-

Table 6
Recommendations on the use of vaccine prevention in the different AML/APL settings.

Vaccine	Recommendations	LoA
Pneumococcal *	Pneumococcal vaccination with 20-valent pneumococcal conjugate vaccine (PCV-20) (single dose) is recommended in all AML patients particularly in older patients (≥ 65 years). It should be administered preferentially before starting antileukemic therapy. If delivery of vaccination is not feasible before therapy start, it can be administered at any time in less intensive treatments and after treatment discontinuation in patients submitted to intensive chemotherapy.	100%
VZV	VZV vaccination with adjuvated recombinant zoster vaccine (two doses at least one month apart) is suggested preferentially before starting antileukemic therapy, particularly in older patients (≥ 65 years). If delivery of vaccination is not feasible before therapy start, it can be administered at any time in less intensive treatments. In patients submitted to intensive chemotherapy particularly if receiving AVP during chemotherapy VZV vaccination can be postponed after chemotherapy discontinuation.	93%
Influenza	Seasonal (once a year) influenza vaccination with adjuvated flu vaccine is recommended particularly in elderly patients.	100%
SARS-CoV-2	SARS-CoV-2 vaccination (at least once a year) is suggested particularly in elderly patients. **	93%
RSV	RSV vaccination may be considered preferably before treatment or after intensive chemotherapy discontinuation.	100%

AML: acute myeloid leukemia; APL: acute promyelocytic leukemia; VZV: varicella-zoster virus; AVP: antiviral prophylaxis; RSV: Respiratory Syncitial Virus; LoA: level of agreement.

* These recommendations have been based on the Italian law context, and, therefore may vary in other jurisdictions.

** As a consequence of epidemiological changes and the spread of potentially vaccine-unresponsive variants, indications on vaccination against SARS-CoV2 may need to be revised soon.

Table 7
Recommendations on PJP prophylaxis and prophylaxis of HBV reactivation in the different AML/APL settings.

Item	Recommendations	LoA
PJP	PJP is infrequently found in AML/APL patients. Recent data about the role of anti-PJP prophylaxis are totally absent. Anti-PJP prophylaxis is not routinely recommended in AML/APL patients, except for selected cases.	100%
HBV *	The panel fully agrees that the use of third-generation antiviral drugs (entecavir, tenofovir or tenofovir alafenamide) is recommended in HBsAg-positive AML/APL patients regardless of HBV DNA levels. Antiviral prophylaxis should be initiated at least 1 week before or in concomitance with starting cytotoxic chemotherapy. It should be continued for the duration of cytotoxic chemotherapy and administered for at least 12 to 24 months after chemotherapy withdrawal. Patients receiving cytotoxic chemotherapy with resolved HBV infection (HBcAb positive, HBsAg negative, HBV DNA negative) should receive antiviral prophylaxis. In recent years international guidelines have proposed the use of third-generation antiviral drugs (entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide), rather than lamivudine, in patients at low risk of HBV reactivation, such as those who are HBsAg-negative/HBcAb-positive and HBV DNA negative undergoing cytotoxic chemotherapy due to resistance profile. In contrast, recent Italian guidelines again recommend the use of lamivudine in hematological HBsAg-negative/HBcAb-positive patients undergoing cytotoxic chemotherapy. Even if entecavir and tenofovir have high potency against HBV and low rates of resistance observed with long-term use, prophylaxis with lamivudine is the favored strategy in HBsAg negative/anti-HBc positive patients. Since the risk of developing lamivudine-resistant strains of HBV is related to baseline levels of HBV DNA, which are usually undetectable in such patients, lamivudine should be potent enough to maintain suppressed HBV replication without risk of virological failure due to the emergence of lamivudine-resistant strains. Furthermore, the decision to use lamivudine for prophylaxis is influenced by Italian reimbursement regulations, which currently do not allow the use of third-generation antiviral drugs (entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide). In HBsAg-negative/HBcAb-positive patients receiving cytotoxic chemotherapy antiviral prophylaxis should be initiated at least 1 week before or in concomitance with starting chemotherapy. It should be continued for the duration of chemotherapy and should be administered for at least 18 months after chemotherapy withdrawal. The panel suggests monitoring HBsAg and HBV DNA assays every 6 months. All HBsAg negative/anti-HBc positive patients who have detectable HBV DNA levels (any level) at baseline who will receive cytotoxic chemotherapy should be managed as HBsAg positive patients and therefore we suggest considering prophylaxis with entecavir or tenofovir instead of lamivudine.	100%

AML: acute myeloid leukemia; APL: acute promyelocitic leukemia; PJP: pneumocystis jirovecii pneumonia; HBV: hepatitis B virus; LoA: level of agreement.

* These recommendations have been based on the Italian law context, and, therefore may vary in other jurisdictions.

negative/HBcAb-positive patients undergoing cytotoxic chemotherapy. Even if entecavir and tenofovir have high potency against HBV and low rates of resistance observed with long-term use, prophylaxis with lamivudine is the favored strategy in HBsAg negative/anti-HBc positive patients. Since the risk of developing lamivudine-resistant strains of HBV is related to baseline levels of HBV DNA, which are usually undetectable in such patients, lamivudine should be potent enough to maintain suppressed HBV replication without risk of virological failure due to the emergence of lamivudine-resistant strains [167]. Furthermore, the decision to use lamivudine for prophylaxis is influenced by Italian reimbursement regulations, which currently do not allow the use of third-generation antiviral drugs (entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide). In HBsAg-negative/HBcAb-positive patients receiving cytotoxic chemotherapy antiviral prophylaxis should be initiated at least 1 week before or in concomitance with starting chemotherapy. It should be continued for the duration of chemotherapy and should be administered for at least 18 months after chemotherapy withdrawal. The panel suggests monitoring HBsAg and HBV DNA assays every 6 months. All HBsAg negative/anti-HBc positive patients who have detectable HBV DNA levels (any level) at baseline who will receive cytotoxic chemotherapy should be managed as HBsAg positive patients and therefore we suggest considering prophylaxis with entecavir or tenofovir instead of lamivudine.

3.6. *Pneumocystis jirovecii pneumonia (PJP) prophylaxis in AML/APL patients*

PJP is infrequently found in AML/APL patients. Trimethoprim/sulfamethoxazole prophylaxis is not routinely administered to AML patients undergoing conventional intensive chemotherapy [172]. Poor data have been recently published since 2012 on PJP incidence in AML, mostly coming from case series and retrospective cohort studies. The most relevant study published so far, the authors reported a PJP incidence of 13.2% among AML patients treated with venetoclax-based regimens [173–176]. Recent data about the role of anti-PJP prophylaxis are totally absent.

PANEL RECOMMENDATION (Table 7). Based on that discussed above, the panel fully agrees that anti-PJP prophylaxis is not routinely recommended in AML/APL patients, except for selected cases.

3.7. *Antimicrobial prophylaxis for oral decitabine/cedazuridine (DEC-C) and menin inhibitors*

Data from recent studies of oral (DEC-C) in AML patients, alone or combined with venetoclax, indicate that infections are a clinically relevant safety concern, with grade $\geq$ 3 febrile neutropenia reported in 14–29% of patients and pneumonia in 7–23%, depending on the study population and treatment [177–180]. Sepsis and other severe infections were less frequent, but infection-related mortality ranged from 1% to 8%. Prophylaxis was not systematically reported in most studies, except in the phase 2 AML study with venetoclax, where all patients received antiviral, antibacterial, and mold-active antifungal prophylaxis [178]. Overall, these studies provide limited detail on the specific causes of infection, and the current evidence does not allow firm conclusions regarding the true infection burden associated with oral DEC-C or the impact of prophylactic strategies. Detailed data have been summarized in Table S10.

PANEL RECOMMENDATION. Based on the studies published so far, the panel fully agrees that there is low evidence to recommend the use of antimicrobial prophylaxis in AML patients receiving oral DEC-C. However, most of the information might be translated from that reported for patients treated with HMA alone. Data on infections and antimicrobial prophylaxis in patients treated with menin inhibitors remain limited and largely derived from early-phase clinical trials not specifically designed to evaluate infection-related outcomes [181–184]. Across available studies, prophylactic strategies are rarely reported, except for one trial in which azole antifungal prophylaxis was mandated in a treatment arm receiving strong CYP3A4 inhibitors [184]. Febrile neutropenia represents the most consistently documented infectious toxicity, with rates ranging from approximately 22% to 37% depending on the agent and study population. Severe infections such as sepsis and pneumonia have been reported with varying frequency, particularly in patients receiving treatment in the salvage setting, where disease-related cytopenias are prominent [181,182]. However, comprehensive infection rates, including bacterial, fungal, and viral events, are seldom provided, and several studies report no detailed infectious adverse events at all. Overall, the current evidence base does not allow firm conclusions regarding the true infection burden associated with menin inhibitors or the impact of prophylactic strategies. As these agents move into broader clinical use and earlier treatment lines, dedicated prospective data will be essential to inform optimal infection prevention, management, and supportive care. Detailed data have been summarized in Table S11.

PANEL RECOMMENDATION. Based on the studies published so far, the panel fully agrees that there is low evidence to recommend the use of antimicrobial prophylaxis in AML patients receiving menin inhibitors.

4. Conclusions and future considerations

In this consensus, we considered the issue of infection prevention (bacterial, fungal, and viral) in light of the development of numerous new drugs in recent years that have significantly changed the short-term prognosis of AML patients, especially those over 65. We also carefully considered how the epidemiology of infections, especially bacterial infections, has changed, with a marked increase in forms caused by multidrug-resistant germs. Of note, we recognize our recommendations are not guidelines, no grade has been provided nor a systematic literature review. In addition, the studies we considered in the literature review were heterogeneous, often retrospective, not specifically designed to evaluate the impact of antimicrobial prophylaxis and some information has been extrapolated since not directly provided. We are aware these factors weaken the strength of our recommendations. All these considerations influenced the board's decisions, which showed a lack of unanimity regarding ABP, with a large proportion no longer believing the use of quinolone prophylaxis is mandatory, as suggested by several international guidelines. Regarding AFP and the use of vaccinations, the board's recommendations are perfectly aligned with the suggestions of international guidelines. AVP is still a largely uncovered issue, but the panel agrees this is not recommended other than in APL patients receiving ATO-based regimes. In the era of new regimens for treating patients with AML, prospective studies focusing on infections are warranted to improve clinical management of our patients and mitigate the risk of life-threatening infections. We strongly believe there is a need for tailored antimicrobial prophylaxis strategies, emphasizing the pivotal role of antimicrobial stewardship, to fully account for the complexity and heterogeneity among AML/APL patients. Future strategies, including the potential use of granulocyte-colony stimulating factors, should abandon the “one-size-fits-all” approach in favor of more personalized methods, which could integrate biomarkers, host-specific factors, and microbiome analysis to improve infection risk stratification and direct prophylactic measures. The role of ABP is still under debate and less appealing because of the current worldwide epidemiologic scenario. New prospective, multicenter, randomized study would likely be necessary to finally define the role of ABP nowadays.

4.1. *Practice points*

- FQ-based ABP reduces febrile and infectious episodes but lacks OS benefit, risks MDR selection and microbiota disruption. There are few data outside intensive chemotherapy settings. The panel agreement is low, recommending careful evaluation rather than routine use.

- AFP with posaconazole is recommended for intensive chemotherapy and venetoclax-based regimens (first 4 cycles); it improves survival, reduces IFD. There are not solid data to recommend AFP in APL, or palliative care.
- There is low evidence for routine AVP in most AML settings; it is strongly recommended for all APL on ATO-based regimens until 6 months post-discontinuation due to high VZV/HSV reactivation risk.
- The panel recommend PCV-20 (pneumococcal), annual influenza (especially ≥65y), annual SARS-CoV-2, and adjuvanted rHZ vaccines in all AML/APL patients, ideally pre-therapy or soon after diagnosis; post-chemo humoral response is poor.
- Entecavir/tenofovir is recommended for HBsAg+ patients (start pre-chemo, continue 12–24 months post); lamivudine for resolved HBV (similar duration). The goal is to prevent life-threatening reactivation potentially interfering with leukemia treatment.
- Routine PJP prophylaxis is not recommended except for select cases.
- There is low evidence for antimicrobial prophylaxis in AML patients treated with oral DEC-C or menin inhibitors.

4.2. Research agenda

- Continuous investigation on epidemiology and risk assessment of infections is required to detect change in the risk profile of infections in AML, in the light of the new regimens.
- Implementation of registries and clinical studies focusing on monitoring of infections in AML/APL are highly recommended.
- New prospective, multicenter, randomized studies would likely be necessary to finally define the current role of antibacterial prophylaxis in this setting of patients.
- There is need for tailored antimicrobial prophylaxis strategies, emphasizing the pivotal role of antimicrobial stewardship, to fully account for the complexity and heterogeneity among AML/APL patients.
- Future strategies should abandon the “one-size-fits-all” approach in favor of more personalized methods, integrating biomarkers, host-specific factors, and microbiome analysis to improve infection risk stratification and direct prophylactic measures.

Authors contribution

FM, CG, LP were the chairmen of the project and wrote the manuscript. All the other authors, experts in the management of infections and of clinical studies in the hematology field, contributed to the literature review, the writing and the final revision of the manuscript.

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Declaration of competing interest

All the authors disclose no financial and personal relationships with other people or organizations that could inappropriately influence the content of this article.

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Appendix A. Supplementary data

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