

# S281 EHA GUIDELINE: ANTIFUNGAL PROPHYLAXIS IN ACUTE MYELOID LEUKEMIA TREATED WITH NOVEL AGENTS

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## **Background:**

Novel therapeutic agents for acute myeloid leukemia (AML) have become available recently. Antifungal prophylaxis is generally recommended during induction remission chemotherapy, however, treatment settings for AML patients have become diverse and the risk-benefit ratio for antifungal prophylaxis in those settings is not well assessed in clinical trials. Due to cytochrome p450 metabolism and its inhibition by antifungal drugs, there is potential for drug-drug interactions (DDI) between novel AML agents and antifungals.

## **Aims:**

To define evidence- or consensus-based recommendations for antifungal prophylaxis for AML patients on treatment with novel agents

## **Methods:**

Experts from the European Hematology Association (EHA) Working Group Infections in Hematology and Cochrane Hematology Group develop an evidence and consensus-based guideline according to the GRADE methodology. The following PICO endpoints for each of the novel agents were formulated: occurrence of fungal infection, prolongation of hospitalization, days on intensive-care unit and mortality due to fungal infection, quality-of-life, and potential drug-drug interactions. Systematic literature review was performed. In three consensus-meetings, recommendations for each novel AML drug and specific setting were formulated.

## **Results:**

The following novel agents for treatment of AML were identified with not all of them being yet licensed for treatment: Hypomethylating agents (HMA; Azacytidine and decitabine), Midostaurin, Venetoclax (+HMA), Lestaurtinib, Gilteritinib, Sorafenib, Quizartinib, Ivosidenib, Enasidenib, Crenolanib, Glasdegib, Sapacitabine, Custatuzumab, Iomab B, Idanasutlin.

Evidence from the literature was generally scarce since fungal infections and prophylaxis were generally not assessed in randomized controlled trials of the respective AML drug.

Evidence-based recommendations were formulated for HMA, Midostaurin, and Venetoclax/HMA, for all other agents, consensus-based recommendations were given including the patient-specific setting of application of the novel agents (relapsed/refractory AML, single therapy or in combination with chemotherapy, induction treatment or maintenance etc.) into the decision process

Antifungal prophylaxis is not recommended or moderately recommended in most settings, and strongly recommended if the novel AML agent is administered with intensive chemotherapy during induction treatment. Dose adaptations of some of the AML agents (midostaurin, venetoclax,

quizartinib, sorafenib, gilteritinib) are moderately recommended with limited evidence if antifungal prophylaxis is administered with a strong CYP3A4 inhibitor due to expected increased exposure

**Conclusion:**

This guideline document to help supporting the decision if to use antifungal prophylaxis in AML patients under treatment with novel agents will soon become available as the first one assessing this specific setting and will complement existing guidelines for antifungal prophylaxis.

**Keyword(s):** Acute myeloid leukemia, Drug interaction, Fungal infection, Prophylaxis