Frontline Antifungal Prophylaxis with Dose-Adjusted Venetoclax Combinations in Patients with Acute Myeloid Leukemia or High-risk Myelodysplastic Syndromes

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BACKGROUND

Older or unfit patients with Acute Myeloid Leukemia (AML) are commonly treated with **venetoclax-based low-intensity regimens**. Due to prolonged neutropenia and invasive fungal infections (IFIs) risk, antifungal prophylaxis is frequently used, although its benefit remains controversial.

At our institution, **frontline azole antifungal prophylaxis with concomitant venetoclax dose adjustment** is routinely used. We conducted a retrospective analysis to evaluate clinical outcomes associated with this strategy.

METHODS

- Single-center retrospective study at a referral hospital in Mexico City.
- Patients (≥18 years) with AML or high-risk myelodysplastic syndrome (MDS),**unfit for intensive chemotherapy** between **2018-2025** were included.
- Treatment: frontline **venetoclax-based therapy** → azacitidine or low-dose cytarabine combined with venetoclax 100 mg/daily, administered 14–28 days + **antifungal prophylaxis with an azole** agent
- **Primary outcomes:** overall survival (OS) and adverse events graded according to CTCAE v5.0.
- **Secondary outcomes:** complete remission (CR) rates, cytopenias, IFIs, and event-free survival.

CONCLUSIONS

Frontline azole antifungal prophylaxis with concomitant venetoclax dose adjustment **was feasible in a highly comorbid population receiving venetoclax-based therapy.**

Despite prolonged cytopenias, the 30-day-mortality remained relatively low, while **remission rates and survival outcomes were comparable** to those reported in pivotal venetoclax-based studies.

RESULTS

- 43 patients (58.1% male); 83.7% with AML; median age: 70 years (IQR 63–79)
- 95.3% had significant comorbidity burden
- Composite remission rate was 65.1%, including 48.8% CR.
- Median Overall Survival: 17.5 months (95%CI 14.5–20.6).
- 30-day mortality was 9.3%
- During induction, 95.3% developed grade 4 neutropenia, 97.7% grade 3 thrombocytopenia, and 18.6% developed IFIs.
- Median duration of severe neutropenia and thrombocytopenia was 30 (IQR 21–36) and 21 days (IQR 16–35), respectively.

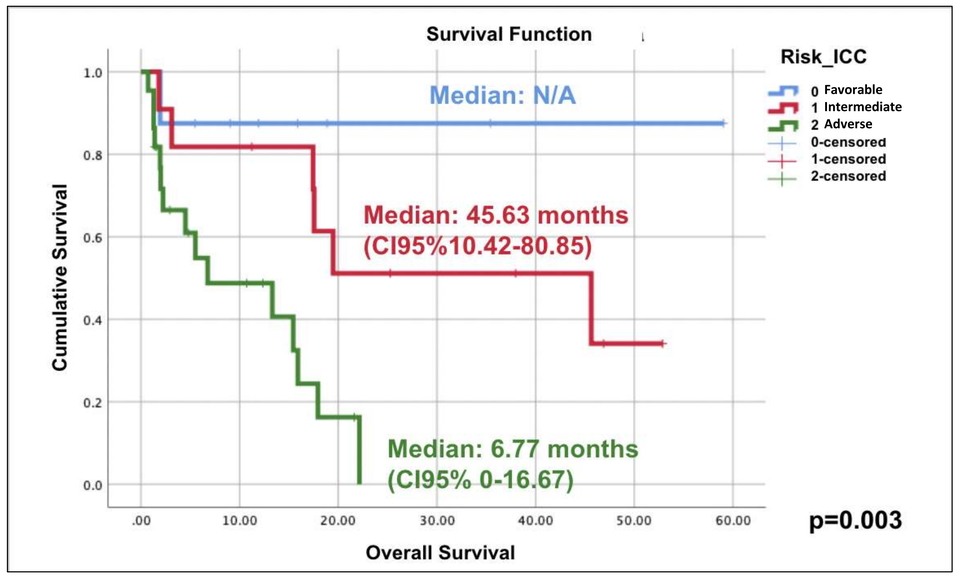

Figure 1. Median Overall Survival according ICC/ELN risk. P=0.003

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REFERENCES

1. DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Wei AH, et al. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 13 de agosto de 2020;383(7):617-29. doi:10.1056/NEJMoa2012971
2. Pollyea DA, Stevens BM, Jones CL, Winters A, Pei S, Minhajuddin M, et al. Venetoclax with azacitidine disrupts energy metabolism and targets leukemia stem cells in patients with acute myeloid leukemia. Nat Med [Internet]. 2018;24(12):1859–66. Disponible en: http://dx.doi.org/10.1038/s41591-018-0233-1
3. Salem AH, Menon RM. Clinical pharmacokinetics and pharmacodynamics of venetoclax, a selective B-cell lymphoma-2 inhibitor. Clin Transl Sci. mayo de 2024;17(5):e13807. doi:10.1111/cts.13807 PubMed PMID: 38778732; PubMed Central PMCID: PMC11112299.
4. Zhong X, Wang J, Dai Y, Huang X, Liu J, Xiang B, et al. Combining azole antifungals with venetoclax plus azacitidine in patients with newly diagnosed acute myeloid leukemia. Hematology. 31 de diciembre de 2024;29(1):2433172. doi:10.1080/16078454.2024.2433172