



Intentional Azole Antifungals with Azacitidine-Venetoclax Based Combination in AML as an Outpatient Therapy: Experience from a Resource-Limited Setting in India

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Introduction

Acute myeloid leukemia (AML) primarily warrants intensive induction therapy, followed by consolidation chemotherapy as a curative regimen.

However, in elderly (>60 years) and unfit younger patients, less-intense regimens with targeted therapy have been effective.

They have proven to be effective regimens for improving overall survival and remission rates while the world battles COVID-19.

Objective

The primary outcome of the study was complete remission(CR) rates.

The secondary objective was to assess the rate of MRD negativity.

Patients & Methods

A retrospective study, where case files for all patients diagnosed with AML at a tertiary care center from 2016–2021 were reviewed.

The study included patients who received a low-intensity regimen for remission induction, either in upfront or relapsed settings.

Study cohort characterized by descriptive statistics.

Baseline Characteristics

Parameter	Value (N=55)
Median age at diagnosis (years)	45 (17-75)
▪ ≥60 years	16 (29%)
Sex, M:F	32:23
ECOG PS >3	24 (43.5%)
Comorbidities	19 (34.5%)
Infections	4 (7%)
Median Duration of symptoms	1.5 (0.25-9months)

Lab. parameter	Value
Hemoglobin(g/dL)	7.7(4-11.6)
TLC (cells/ μ L)	13930(730-280930)
Platelets (cells/ μ L)	49000 (10000-471000)
PS Blasts %	60%(2-96)
FAB classification	M2(42.5%)
WHO classification	AML-NOS (46.3%)
Abnormal Karyotype	5 (9%)

Results

Azacitidine was used in 52.7% (induction+maintenance), azacitidine and venetoclax (aza-ven) in 34.5%, and low-dose cytarabine in 14.5%.

In the aza-ven cohort, patients received itraconazole (n=15/19, 78.9%) and voriconazole (n= 4/19, 21.5%) as azoles.

Figure 1: Complete response rates (CR)

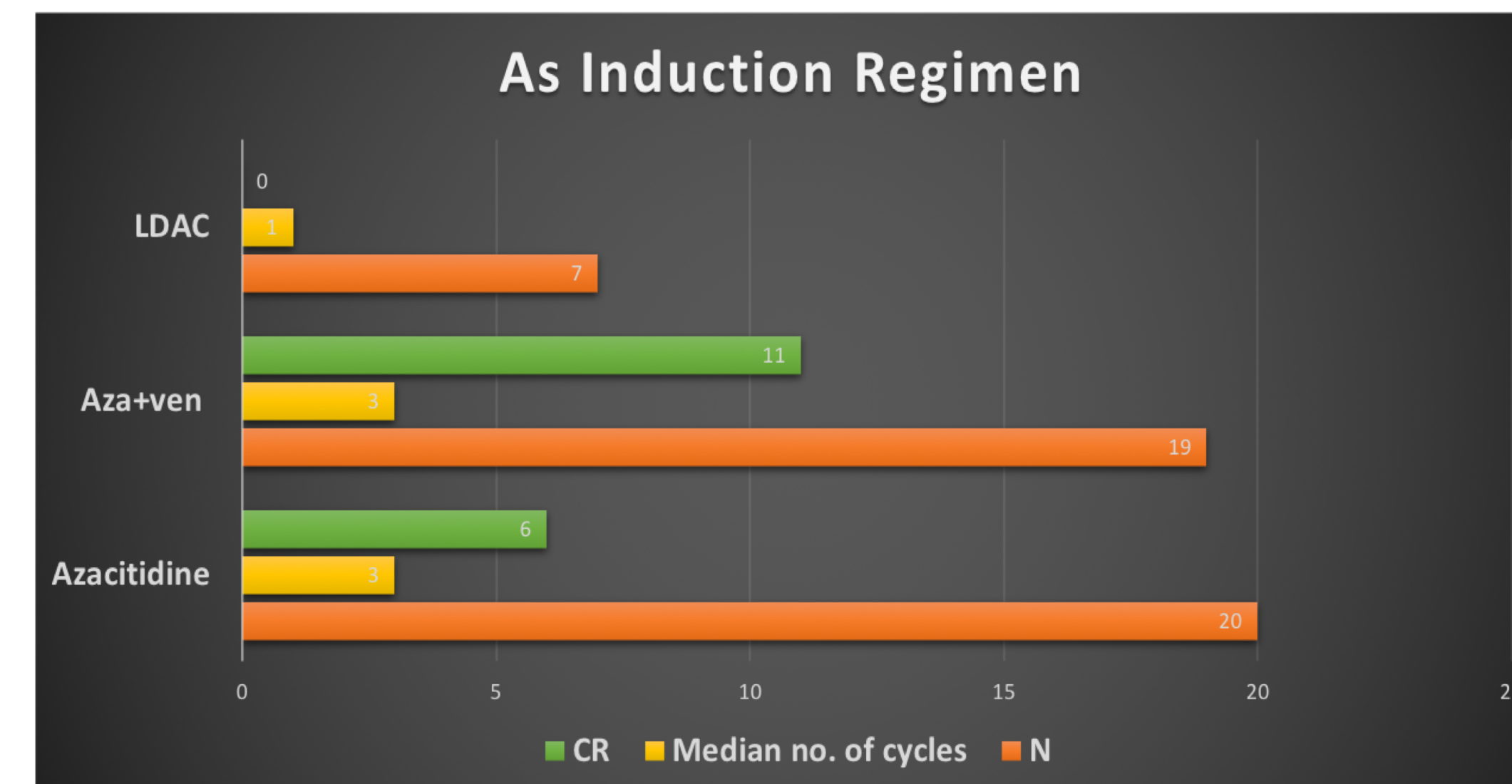
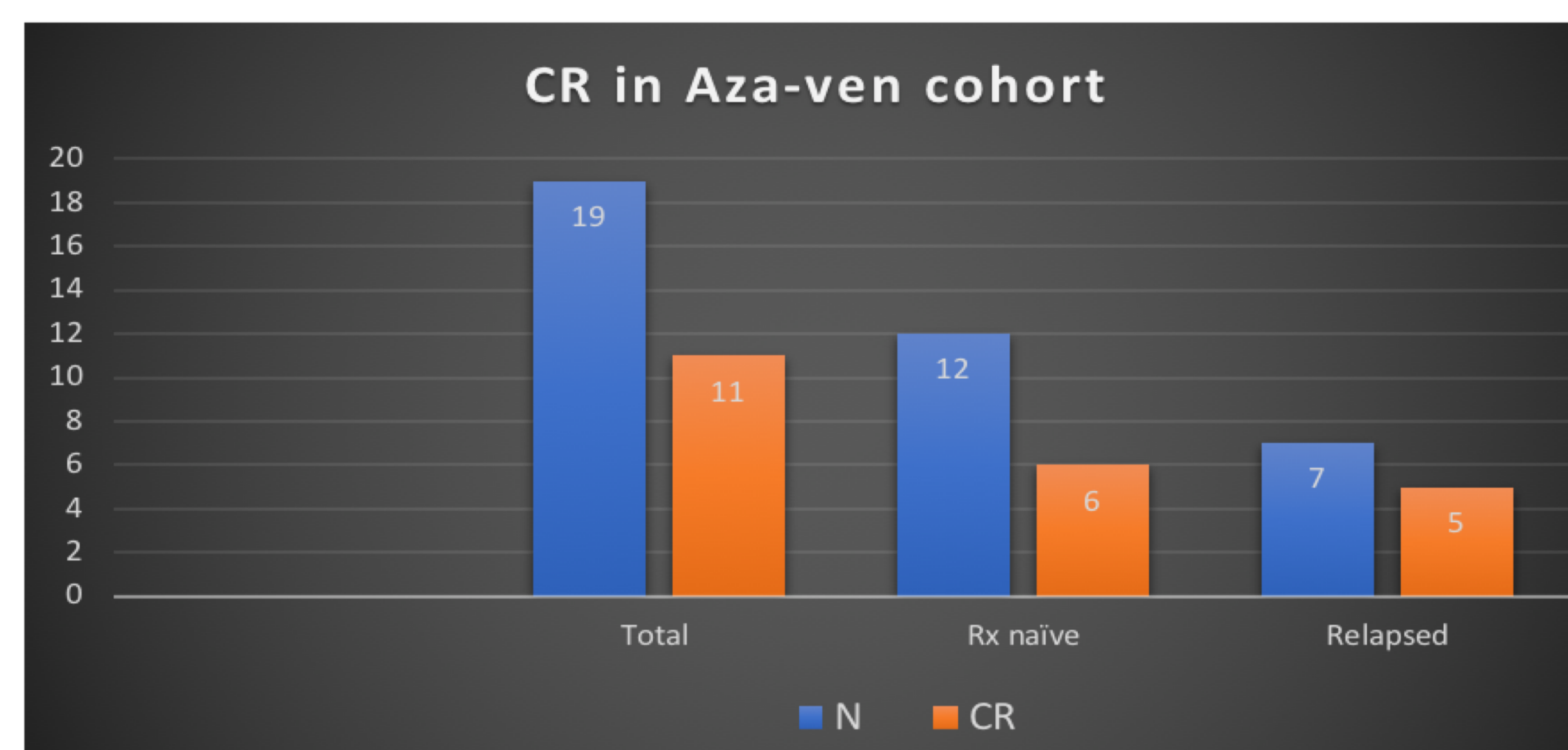


Figure 2: Complete response rates (CR) in Aza-Ven



Discussion

The dose of venetoclax was reduced as azoles were used simultaneously. Dosing varied from 100 to 200 mg and no ramp-up was used.

None of the patients developed tumour lysis syndrome. Patients were initiated with remission induction in an outpatient setting.

The complete remission rates (CR+CRi) in the aza-ven cohort were 50% and 71% in treatment-naïve and relapsed/refractory settings, respectively.

The incidence of febrile neutropenia and fungal infection (probable/possible/proven) were 16.6% and 16%, respectively.

The most common adverse affect was deranged liver function tests with azoles.

Azacitidine was primarily used as maintenance therapy. Interestingly, MRD+ patients (3/10) attained MRD negativity after two cycles, accounting for 100% remission status (10/10).

It bridged the gap, allowing four previously unfit patients to receive intensive chemotherapy and two to receive haploidentical stem cell transplant.

Conclusion

This retrospective study highlights the importance of low-intensity therapy, especially during COVID-19.

Aza-ven-azole is a safe and feasible remission induction regimen in patients who are ineligible for intensive induction which can be consolidated with intensive regimen later.

References

- DiNardo CD, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617-629.
- DiNardo CD, Pratz K, Pullarkat V, et al Venetoclax combined with decitabine or azacitidine in treatment-naïve, elderly patients with acute myeloid leukemia. Blood 2019;133:7-17.