Real World Practice of FLAG-Idarubicin-Venetoclax in Relapsed/Refractory Acute Myeloid Leukemia (AML): A Single Center Experience

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Background

Outcomes of patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) remain poor. Only a small fraction achieve second remission and undergo allogeneic transplantation with long term survival. The FLAG-Ida-Ven combination has shown promise in a phase I/II for patients with R/R AML reported by DiNardo et al. with ORR 70%; 61% achieved composite CR and 69% of those had MRD negativity. Infectious complications remain a concern, with median count recovery of 37 days in this setting.

Design

The objective was to describe the patient population, outcomes, and adverse events of those receiving FLAG-Ida-Ven for R/R AML.

A retrospective chart review was performed at a single, major academic bone marrow transplantation center from August 2019 to December 2021. This included adults with relapsed/refractory AML receiving regimen of interest. Main outcomes measured include overall response rate, MRD status, overall survival, and transition to HSCT.

Patient Characteristics

FLAG-IDA-VEN (n=31)	
Age at Treatment (Years)	50.6 (±16.5) Median 53
Sex (Male)	21 (68%)

Disease	N (%)
Prior MDS/MPN	10 (23%)
TP53 mutated	10 (23%)
Prior allo-HSCT	6 (19%)

European Leukemia Net (ELN) Risk	N (%)
Favorable Risk	1 (3%)
Intermediate Risk	9 (29%)
Adverse Risk	20 (65%)

Patient Characteristics

Treatment Prior to Flag-Ida-Ven	N
Median Prior Lines of Therapy	2 (1-6)
Received Prior Intensive Chemotherapy	9 (29%)
Received Prior HMA+Ven	6 (19%)
Received Prior Intensive Chemotherapy and HMA+Ven	13 (42%)
Failed 3+ lines of treatment	8 (26%)

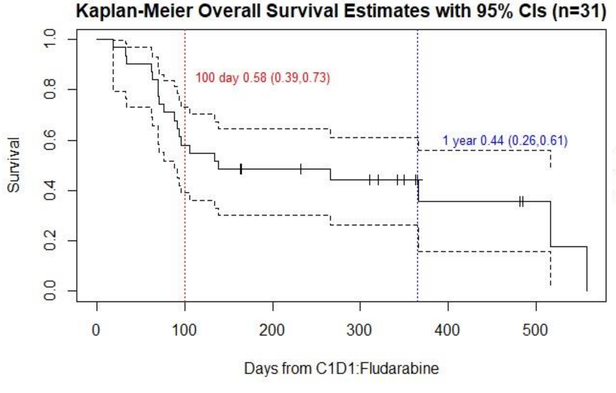


Figure 1. OS estimates of all patients, from day of first fludarabine administration. Of the 31 patients treated in this time period, 20 have expired. Estimated median survival is 138 days (95% CI: 88, 516), survival 100-days post-treatment is 58% (95% CI: 0.39, 0.73), and survival at 1-year post-treatment is 44% (95% CI: 0.26, 0.61).

Descriptive Outcomes

Descriptive Outcomes	N
Achieved MLFS	14/30 (46%)
MRD Negative	12/30 (40%)
No Response to FLAG-IDA-VEN	12 (39%)
Relapsed After FLAG-IDA-VEN	5 (16%)
Mean Time to ANC>500 Recovery from C1D1, if recovered (days)	36.7 (±20.4) Median 35
Mean Time to Platelets >50,000 from C1D1, if recovered (days)	51.6 (±42.8) Median 38.6
Successful Taken to Transplant	13 (42%)
Time to Transplant from C1D1 (Days)	86.9 (50-151), median 89
TMLI–based Conditioning Regimen	3 (23%)

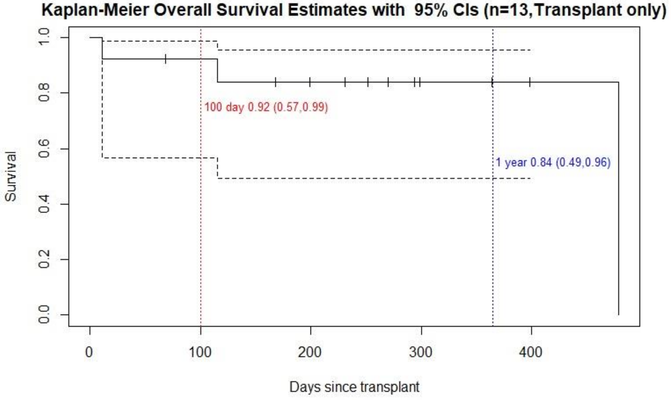


Figure 2. OS estimates of patients taken to allogeneic HSCT. Of the 13 patients, 3 have expired as of data-lock date. Estimated median survival time is 479 days (95% CI :115, N/A). Survival at D+100 post-HSCT is 92% (95% CI: 0.57, 0.99), and survival at 1-year post-transplant is 84% (95% CI: 0.49, 0.96).

Infection and Mortality

Confirmed Infection	13 (42%)
Bacteremia	16 (52%)
Pneumonia	10 (23%)
Invasive Fungal Infection	10 (23%)
Time of Infection from C1D1 (days)	33 (±15) Median 28
Febrile Neutropenia	23 (74%)
ICU Transfer During Same Admission	5 (16%)

Mortality at Cut-Off	20 (65%)
30-Day Mortality	1 (5%)
100-Day Mortality	13 (65%)
Time to Death from C1D1 (days)	147.7 (±155) Median 90

HSCT	N=13
Median OS	252d (11-479)
D100 OS	11 (85%)

Discussion

14/30 patients achieved blasts <5% in the BM (10 with MLFS, 3 with CR, 1 CRp; and 12/14 had MRD negativity. The median time to ANC recovery >500 was 35 days (20-67) and infectious complications were significant. With a median follow up of 342 days, 20/31 (65%) of patients died. 13/30 (42%) were transplanted at a median time of 87 days (50-151). Of the 13 patients who were transplanted 11/13 were alive at Day +100, with an estimated 1-year OS of 84% (95%CI: 0.49,0.96).

FLAG-Ida-Ven is an effective regimen in the R/R setting for appropriately selected patients and may be a bridge to transplant with MRD negative remission. Infectious complications and count recovery remain a challenge and should be strongly considered as regimen related toxicity.

References

1. DiNardo CD, Lachowiez CA, Takahashi K, et al. Venetoclax Combined With FLAG-IDA Induction and Consolidation in Newly Diagnosed and Relapsed or Refractory Acute Myeloid Leukemia. J Clin Oncol. 2021 Sep 1;39(25):2768-2778.