The Effect of Comorbidities and Choice of Treatment on Overall Survival in Elderly Patients with Acute Myeloid Leukemia: A Beaumont Experience

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Introduction

Acute myeloid leukemia (AML):

- classified as a systemic proliferation of premature cells within the myeloblast lineage.
- These cells are unique in that they are at immature stages and result in the accumulation of blast cells.[1]
- Acute Myeloid Leukemia (AML) is primarily a disease of the Elderly
- Elderly Patients have **multiple comorbidities leading to Poor Outcomes**[1]

Main Treatment Strategy: 7+3 Regimen[2]

- **7 days of invasive Cytarabine and 3 days of Anthracycline**
- Complete Remission (CR) in 40-60%[2]
- **Only 10% Five year survival rate**[2]
- **Restricted** in patients with comorbidities[2]

New option: **BCL-2 Antagonists: Venetoclax (Ven)**

- Developed for CLL[3]
- Little effect on AML
- **When combined with Hypomethylating agents (HMA) some success in treating AML[4,5]**
- **Used in patients with multiple comorbidities and can't withstand treatment with 7+3 regimen**

Hypothesis: Elderly AML patients who receive Venetoclax with a hypomethylating agent will have worse survival outcomes since it is used in patients with greater comorbidities.

Aims and Objectives

- This capstone project aims to understand the various treatment protocols that can be implemented in elderly patients with Acute Myeloid Leukemia (AML) at the Beaumont Health System.
- The rationale for this research is to determine the effectiveness of the use of Venetoclax with Hypomethylating agents vs the standard 7+3 protocol in the Beaumont Health System.
- This will help us in determining the best standard protocol for treatment of elderly patients with AML. This will be determined by comparing survival outcomes of the patients in both treatments.

Aim 1: Compare survival outcomes for patients treated in both therapeutic regimens.

Aim 2: Understand added complications of cytogenetics, gender, and age and their effects in survival outcomes of patients based on the two regimens.

Aim 3: Determine whether Venetoclax with Hypomethylating agents is being used appropriately, specifically in patients with higher comorbidities.

Methods

- Retrospective chart review using Electronic Medical Record at Beaumont Health Royal Oak and Troy.
- Inclusion criteria: patients seen by Beaumont Hematology and Oncology Group that were
  - 60 or older diagnosis of AML by bone marrow biopsy who received treatment for AML.
  - Patients were seen between 09/2019 and 09/2020.
- Sample Size:
  - 23 Patients received 7+3 regimen
  - 26 Patients received HMA/Venetoclax
- Variable of Interest:
  - Date of diagnosis
  - Date of death
  - Number comorbidities:
  - Type of treatment
  - Age
  - Molecular Abnormalities
  - Survival outcome

Results

- Of the 23 patients who received 7+3 initial treatment, 13 passed away with a median time of death of 1.98 years,
- Of the 26 patients who received HMA/Ven as the initial treatment, 17 passed away with a median time of death of 0.71 years (P-value .039).
- The initial treatment of HMA/Ven was associated with 2.19-fold greater hazard of mortality as compared to 7+3 (HR:2.19; P = 0.0403).
- When comparing which treatment was chosen for those with comorbidities and age, those that received the initial treatment of 7+3 had less comorbid conditions (4.5 versus 6.1; p=0.04), and were younger (62 versus 75.5; p<0.0001) than those that did not receive the initial treatment of 7+3.

Table 1: Variables stratified by mortality status

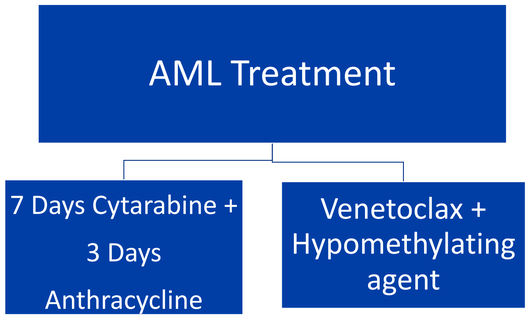
Variables	Deceased	Living	Hazard Ratio (95% CI)	P-value
Mean # of comorbid conditions	5.6 (2.3)	5.0 (3.7)	1.05 (0.93-1.17)	0.42
Mean Age (SD)	67.6 (12.2)	66.3 (11.6)	1.02 (0.99-1.05)	.0329
IDH+ IDH-	9 (30%) 21 (70%)	3 (15.8%) 16 (84.2%)	1.24 (0.93-1.17)	0.527
Initial Treatment n (%): 7+3 HMA/Ven	13 (43.3%) 17 (56.7%)	10 (52.6%) 9 (47.4%)	2.19 (1.02-4.68)	0.040

Table 2: Analysis of variables stratified by treatment type

Variables	7+3 Treatment (N=23)	HMA/Ven Treatment (N=26)	P-value
# of Deaths Median time to death	13 1.98	17 0.71	0.0393
Mean # of comorbid conditions	4.5 (2.4)	6.1 (3.1)	0.0441
Mean Age	62	75.5	0.0001
IDH + IDH -	6 (26.1%) 17 (73.9%)	6 (23.1%) 20 (76.9%)	1.000

Conclusions

- Median survival for those who received HMA + Venetoclax was less than those who received 7+3.
- HMA + Venetoclax was used in patients who were older and had more comorbidities.
- There was no statistically significant difference in mortality status when compared with number of comorbidities, age, and IDH molecular abnormalities
- There was no statistically significant difference in treatment type used when compared with the presence of IDH molecular abnormalities
- Our hospital was using this in the appropriate patients; those who were older or had more comorbidities.



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