Utilization of Hypomethylating Agents and Associated Outcomes in Elderly Acute Myeloid Leukemia (AML) Patients: A Population Based Study

Maneesha Mehra[1*], Jianming He[1], Ravi Potluri[2], Christina Loefgren[1]

[1]Janssen Global Services LLC, Raritan, NJ; [2]SmartAnalyst Inc., New York, NY

*Presenting Author

INTRODUCTION:

- Acute myeloid leukemia (AML) is more common in the elderly population with an estimated median age of 70 years at diagnosis.[1]
- Intensive chemotherapy is the standard of care for AML. The National Comprehensive Cancer Network (NCCN) recommends high-intensity induction therapy for patients aged ≥ 60 years only in limited circumstances.[2-4] However, long term survival in elderly patients treated with intensive chemotherapy remains low due to high risk of relapse and mortality. The prognosis is even worse in patients who are ineligible for intensive chemotherapy and treated with only supportive care.[2]
- Hypomethylating agents (HMAs) like decitabine and azacitidine may be helpful in improving overall survival and quality of life in elderly patients with AML who are ineligible for intensive chemotherapy; however, limited comparative data are available regarding survival benefits with HMAs.
- This population based study was conducted to compare the survival outcomes between decitabine and azacitidine in elderly patients with AML. Outcomes were compared by using data from the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database.

METHODS:

Study design and sample selection

- This was a retrospective cohort analysis performed on AML patients identified through the linked SEER-Medicare database, a linkage of two large population-based data sources that provide detailed information about beneficiaries with cancer.
- Since, Medicare's eligibility is restricted largely to the elderly population, the linked database was well suited for the study.

Inclusion criteria

- Patients who had index AML diagnosis between January 1, 2007 and December 31, 2014
- Enrollment in Medicare Part A and Part B at the time of index diagnosis

Exclusion criteria

- Enrollment in Medicare Advantage at the time of index diagnosis

Assessments of variables

- Utilization pattern of most common AML regimens was assessed by lines of therapy (LOTs). LOTs were categorized as LOT1, LOT2, LOT3, and LOT4+.
- Survival analysis was performed for patients receiving decitabine or azacitidine as first line therapy (LOT1), and separately, as second line therapy (LOT2).
- There were three possible sources of death dates for a patient in the SEER-Medicare database: Medicare enrollment database, SEER registry, and Inpatient death. If death date was reported from more than one source for a patient, the above hierarchy was used to assign the death date for analysis.
  - If death date was available as per the above criteria, it was considered as an event; if it was not available, patient was censored on the study end date, 31 December 2014.
  - Duration of survival for the analysis for a patient was taken to be from the start of treatment of LOT to event or censoring date, whichever was the case.

Statistical analysis

- Descriptive statistics were reported for the demographics and baseline characteristics, and distribution of most common regimens by LOTs.
- Kaplan-Meier analysis and Cox proportional hazards regression were used to assess the overall survival by treatment. Kaplan-Meier analysis was stratified by age groups (<75 years and ≥75 years). The Cox proportional hazards model was adjusted for potential confounders such as treatment, age, gender, time to treatment, and transfusion status before treatment initiation.

RESULTS:

- A total of 9445 patients with AML met the inclusion criteria. Of these, 3922 patients received LOT1 treatment, and 1582 patients received LOT2.

Demographics and baseline characteristics

- A majority of the LOT1 patients were Caucasian (85%) and women (57%).
- A significant difference between the mean age of decitabine (74.3 years) and azacitidine (75.1 years) cohorts (p=0.0139) was observed.
- There was no association between race and selection of HMA (HMA type) (p=0.8431) or gender and HMA type (p=0.5423) in the LOT1.

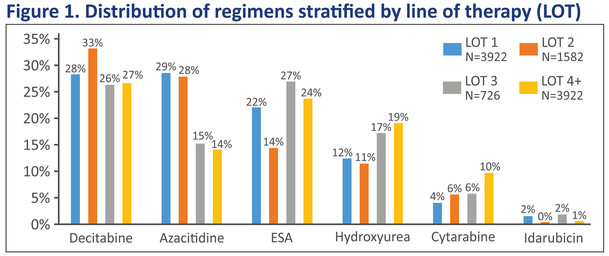
Table 1. Patient demographics

Category	Patients with LOT1 (N= 3922)	Decitabine (N=1110, 28%)	Azacitidine (N=1122, 29%)
Age, years			
Mean (SD)	74.9 (8.9)	74.3 (8.1)	75.1 (7.9)
Race, n (%)			
Caucasian	3339 (85.1)	954 (85.9)	985 (87.8)
African American	248 (6.3)	68 (6.1)	62 (5.5)
Other	335 (8.5)	88 (7.9)	75 (6.6)
Gender, n (%)			
Women	2237 (57.0)	443 (39.9)	462 (41.2)
Patients with a prior transfusion, n (%)	2025 (52.0)	633 (57.0)	599 (53.0)

Utilization of HMAs

- Among patients with LOT1, 1110 (28%) received decitabine and 1122 (29%) received azacitidine, while among LOT2 patients, 522 (33%) received decitabine and 443 (28%) received azacitidine.
- Both HMAs had high utilization (>50%) in LOT1 with comparable consumption (decitabine: 28%, azacitidine: 29%).
- In LOTs subsequent to LOT2, decitabine maintained high utilization pattern however, azacitidine failed to show the same trend.
- Decitabine (27%) and azacitidine (24%) were the most commonly used AML regimens across all lines of therapies.
- The average treatment duration for decitabine and azacitidine was comparable and longest for LOT 1 (decitabine: 116 days; azacitidine: 122 days; p=0.3305) and LOT 2 (decitabine: 104 days; azacitidine: 119 days; p=0.1907).

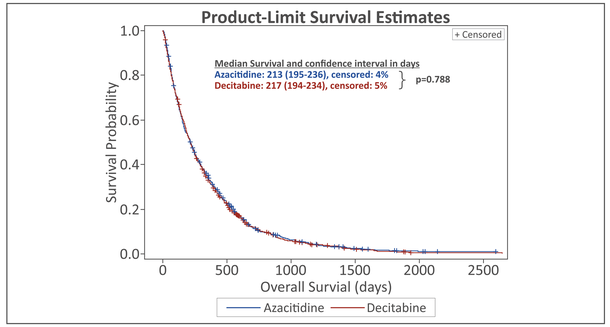
Figure 1. Distribution of regimens stratified by line of therapy (LOT)



Overall Survival

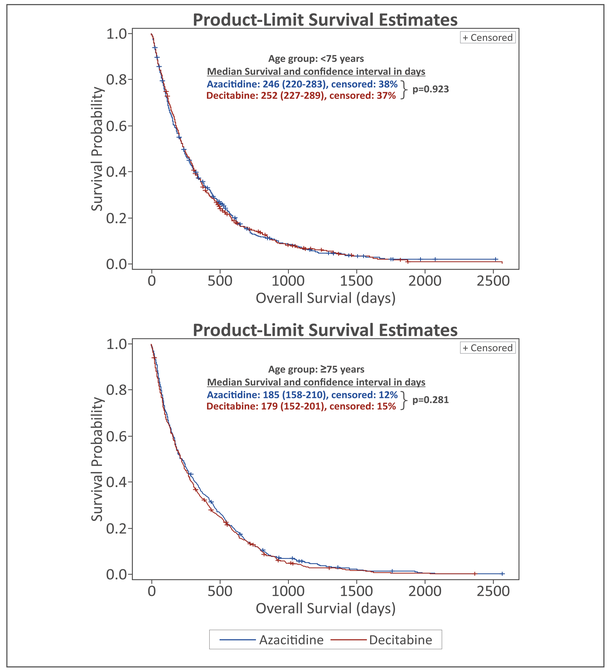
- The median overall survival (mOS) was comparable (p=0.7878) between the patients treated with decitabine (217 days, 95% CI: 194-234) and azacitidine (213 days, 95% CI: 195-236) as LOT 1.

Figure 2. Overall survival of decitabine vs azacitidine in first line of therapy (LOT 1)



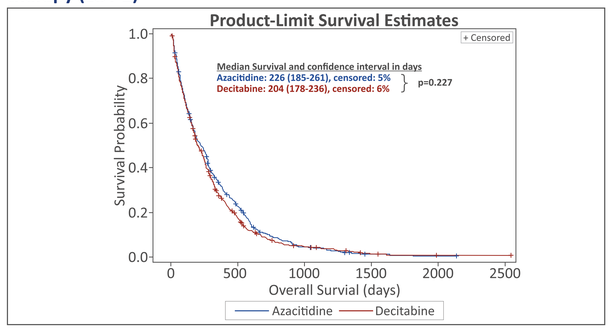
- The mOS did not differ in both treatments by age group: <75 years (decitabine: 252 days, 95% CI: 227-289; azacitidine: 246 days, 95% CI: 220-283, p=0.9228) vs ≥75 years (decitabine: 179 days, 95% CI: 152-201; azacitidine: 185 days, 95% CI: 158-210, p=0.2805).

Figure 3. Overall survival of Decitabine vs Azacitidine in first line of therapy (LOT 1) by age groups



- Similar mOS was observed (p=0.2268) in patients who received decitabine and azacitidine as LOT 2 (decitabine: 204 days, 95% CI: 178-236 vs azacitidine: 226 days, 95% CI: 185-261).

Figure 4. Overall survival of decitabine vs azacitidine in second line of therapy (LOT 2)



- Multivariate Cox proportional hazards analysis showed significantly lower survival benefit with lesser age (HR: 1.02, p <0.0001) and transfusion independence at the time of diagnosis (HR: 1.31, p<0.0001).
- No difference in the risk of death was observed between both HMA treatments (HR: 1.02, p=0.65) when adjusted for age, gender, time to treatment and transfusion status.

Table 2. Cox proportional hazard model showing predictors of overall survival in line of therapy (LOT 1)

Prognostic Variable	Hazard Ratio	95 % CI	p value
Treatment Type (Decitabine vs. Azacitidine)	1.020	0.937, 1.111	0.6507
Age (in years)	1.024	1.018, 1.03	<.0001
Gender (Men vs. Women)	1.046	0.959, 1.14	0.3111
Time to treatment (in months)*	1.004	0.996, 1.011	0.3292
Transfusion status before treatment initiation (Yes vs No)**	1.309	1.2, 1.427	<.0001

*Time to treatment was measured (in months) from index AML diagnosis date to LOT 1 start date.
**Transfusion status (=Yes) was based on the presence of at least 1 claim for RBC transfusion before LOT 1 start date. This variable was treated as a proxy variable for transfusion dependent MDS diagnosis before LOT 1 treatment for AML was initiated.

CONCLUSION:

Results of this retrospective registry-based analysis suggest that both decitabine and azacitidine have high utilization in patients with AML. They have comparable survival outcomes and treatment duration for the management of elderly patients with AML who are considered ineligible for intensive chemotherapy.

REFERENCES:

1. Estey E, Dohner H. Lancet. 2006;368(9550):1894-907.
2. Al-Ali HK, Jaekel N, Niederwieser D. J Geriatr Oncol. 2014;5(1):89-105.
3. Smith BD, Beach CL, Mahmoud D, Weber L, Henk HJ. Exp Hematol Oncol. 2014;3:10
4. Medeiros BC, Satram-Hoang S, Hurst D, Hoang KQ, Momin F, Reyes C. Ann Hematol. 2015;94(7):1127-38.

Acknowledgements

The authors thank Dr. Rishabh Pandey (SIRO Clinpharm Pvt. Ltd.) for providing writing assistance and Dr. Harry Ma (Janssen Research & Development, LLC) for providing additional editorial support for this poster.

Disclosures

MM, JH, and CL are employees of Janssen Research and Development, LLC. RP is an employee of SmartAnalyst Inc., contracted by Janssen to assist with the study.

Funded by Janssen Research & Development, LLC, USA

Presented at 59th American Society of Hematology (ASH) Annual Meeting & Exposition, Dec 09-12, 2017, Atlanta, GA.