EE86

Healthcare resource utilization and associated costs among patients with acute myeloid leukemia treated with oral azacitidine as maintenance and those eligible but not treated using a US claims database

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Introduction

- Patients with newly diagnosed acute myeloid leukemia (ND-AML) usually receive frontline intensive chemotherapy (IC) if eligible, with the aim of attaining complete remission (CR)[1]
  - Although most patients achieve CR with IC, relapse remains a risk even after consolidation or hematopoietic stem cell transplantation (HSCT)[1]
- Lower-intensity maintenance therapies may prolong remission and extend survival of patients treated with frontline intensive treatment[2,3]
  - Oral azacitidine (Oral-AZA) showed significant improvements in relapse-free survival (RFS) and overall survival compared with placebo in the QUAZAR AML-001 trial,[4] and is recommended as maintenance treatment by both NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[5] and European LeukemiaNet[6] guidelines for patients with AML in remission following IC who are not candidates for HSCT
  - Healthcare resource utilization (HCRU) and costs associated with Oral-AZA maintenance treatment compared with a "watch-and-wait" approach have not been well characterized in the literature

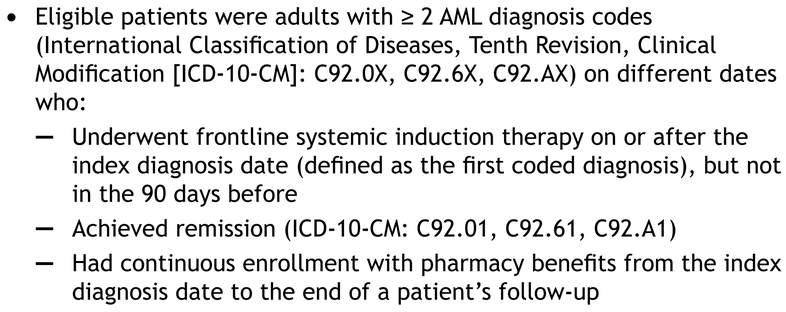
Objective

- To characterize patient characteristics, HCRU, and costs among those with ND-AML who attained remission after treatment with IC and received Oral-AZA maintenance therapy compared with those who did not receive any maintenance treatment in US clinical practice

Methods

- This was a retrospective, observational cohort study of patients with ND-AML in the IQVIA PharMetrics Plus claims database, a longitudinal database of adjudicated medical and pharmacy claims from US health plans
- Eligible patients were adults with ≥ 2 AML diagnosis codes (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]: C92.0X, C92.6X, C92.AX) on different dates who:
  - Underwent frontline systemic induction therapy on or after the index diagnosis date (defined as the first coded diagnosis), but not in the 90 days before
  - Achieved remission (ICD-10-CM: C92.01, C92.61, C92.A1)
  - Had continuous enrollment with pharmacy benefits from the index diagnosis date to the end of a patient's follow-up
  - Received Oral-AZA (Oral-AZA cohort) or no AML maintenance treatment (NoMaint cohort) from remission to disease relapse or end of follow-up (if no relapse)
  - Had an Oral-AZA start date (Oral-AZA cohort) or maintenance eligibility date (MaintDate) (NoMaint cohort) on or after September 1, 2020; MaintDate was defined as the remission date or the day after the last day of consolidation if consolidation therapy was used after remission
- Patients were excluded if they had acute promyelocytic leukemia, or were treated with arsenic trioxide or tretinoin any time during follow-up, or if they received HSCT before the MaintDate
- The end of the follow-up period was the earlier of the HSCT date or the end of continuous insurance enrollment
- The study design is shown in **Figure 1**

Figure 1. Study design



[a]Relapse or HSCT are not necessary conditions for inclusion in the cohorts.

- For descriptive analysis, categorical variables were analyzed as counts and percentages, and compared using chi-square tests; continuous variables were summarized using means, standard deviations (SD), ranges, and percentiles, and compared using t-tests
- For comparative analysis of Oral-AZA and NoMaint cohorts, patients were 1:3 propensity-score matched (based on characteristics at MaintDate)
  - Doubly robust estimates were obtained via a generalized linear model with a gamma distribution (for costs) and negative binomial distribution (for HCRU) with a logarithm link function
- Time to relapse was analyzed from MaintDate until relapse (event) or end of follow-up (censoring), whichever occurred first, using Kaplan–Meier methodology
- HCRU and costs are presented on a per-person per-month (PPPM) basis for overall outpatient, inpatient, and emergency department (ED) visits
  - Costs were payer-adjudicated costs adjusted to 2022 US dollars (USD) using the medical component of the US Consumer Price Index[7]

Results

Patient characteristics

- Following propensity-score matching, 43 patients were included in the Oral-AZA cohort and 129 in the NoMaint cohort; the cohorts were well balanced on all matched variables (**Table 1**)
  - Mean (SD) age in the Oral-AZA cohort was 58.3 (12.4) years and 54.9 (13.9) years in the NoMaint cohort; 48.8% and 54.3% of patients were female in the Oral-AZA cohort and NoMaint cohort, respectively

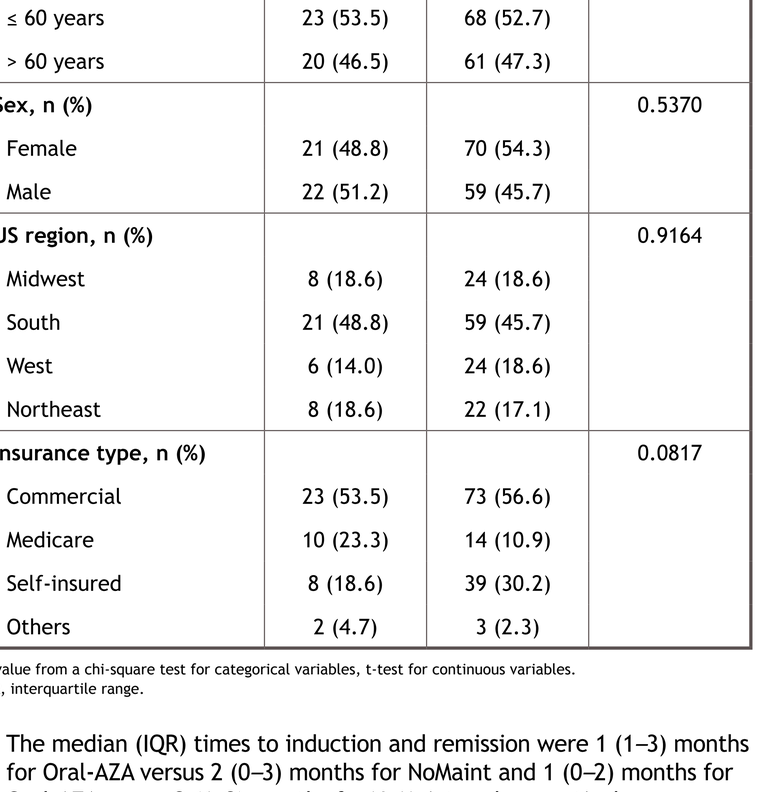
Table 1. Matched patient characteristics at baseline

Characteristics	Oral-AZA (n = 43)	NoMaint (n = 129)	*P* value[a]
Age at MaintDate, years			0.1534
Mean (SD)	58.3 (12.4)	54.9 (13.9)	
Median (IQR)	60 (49-69)	58 (46-64)	
Age group, n (%)			0.9297
≤ 60 years	23 (53.5)	68 (52.7)	
> 60 years	20 (46.5)	61 (47.3)	
Sex, n (%)			0.5370
Female	21 (48.8)	70 (54.3)	
Male	22 (51.2)	59 (45.7)	
US region, n (%)			0.9164
Midwest	8 (18.6)	24 (18.6)	
South	21 (48.8)	59 (45.7)	
West	6 (14.0)	24 (18.6)	
Northeast	8 (18.6)	22 (17.1)	
Insurance type, n (%)			0.0817
Commercial	23 (53.5)	73 (56.6)	
Medicare	10 (23.3)	14 (10.9)	
Self-insured	8 (18.6)	39 (30.2)	
Others	2 (4.7)	3 (2.3)	

[a]*P* value from a chi-square test for categorical variables, t-test for continuous variables.
IQR, interquartile range.

- The median (IQR) times to induction and remission were 1 (1–3) months for Oral-AZA versus 2 (0–3) months for NoMaint and 1 (0–2) months for Oral-AZA versus 2 (1–3) months for NoMaint and respectively
- The mean (median) follow-up was 9.1 (6.0) months for the Oral-AZA cohort and 3.4 (2.0) months for the NoMaint cohort
- The median (95% confidence interval [CI]) time to relapse was significantly shorter in the NoMaint cohort compared with the Oral-AZA cohort (3.3 months [0.8–not reached (NR)] vs median NR [9.0–NR] respectively; *P* = 0.0025) (**Figure 2**)

Figure 2. Kaplan-Meier time to relapse from MaintDate



The Kaplan-Meier analysis was conducted from MaintDate to relapse (event) or the end of follow-up (censoring).

HCRU and costs

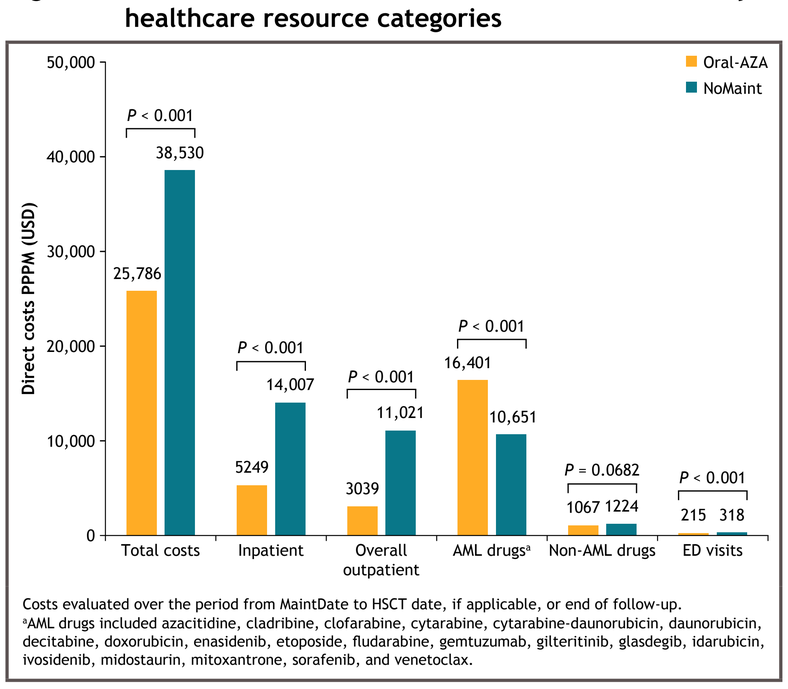
- The mean number of inpatient and overall outpatient visits PPPM was significantly lower in the Oral-AZA cohort than in the NoMaint cohort, and ED visits were comparable for both cohorts (**Table 2**)
- AML drug costs were USD 16,401 PPPM (Oral-AZA treatment accounted for USD 9222) in the Oral-AZA cohort; USD 10,651 PPPM in the NoMaint cohort (**Figure 3**)
- Total costs PPPM were USD 25,786 and USD 38,530 in the Oral-AZA and NoMaint cohorts, respectively (difference, USD 12,744); this difference was driven primarily by inpatient and overall outpatient visits (**Figure 3**)

Table 2. HCRU

Resource use PPPM	Oral-AZA (n = 43) mean (95% CI)	NoMaint (n = 129) mean (95% CI)	Less HCRU by Oral-AZA cohort, %	*P* value
Number of inpatient visits	0.23 (0.15-0.36)	0.61 (0.44-0.83)	62.3	0.0005
Number of overall outpatient visits	5.77 (4.65-7.18)	7.58 (6.59-8.71)	23.9	0.0391
Number of ED visits	0.32 (0.20-0.52)	0.35 (0.25-0.49)	8.6	0.7584

Evaluated over the period from MaintDate to HSCT date, if applicable, or end of follow-up. Differences between the 2 cohorts statistically significant for all resource categories, other than ED visits.

Figure 3. Direct healthcare costs: total costs and costs of key healthcare resource categories



Costs evaluated over the period from MaintDate to HSCT date, if applicable, or end of follow-up.
[a]AML drugs included azacitidine, cladribine, clofarabine, cytarabine, cytarabine-daunorubicin, daunorubicin, decitabine, doxorubicin, enasidenib, etoposide, fludarabine, gemtuzumab, gilteritinib, glasdegib, idarubicin, ivosidenib, midostaurin, mitoxantrone, sorafenib, and venetoclax.

Conclusions

- This study showed lower all-cause HCRU and costs PPPM in a US claims database among patients with ND-AML receiving Oral-AZA maintenance therapy versus matched patients without maintenance treatment
- Higher AML-related drug costs were offset by lower medical costs in the Oral-AZA cohort
- Differences in costs were primarily driven by fewer inpatient and overall outpatient visits among the Oral-AZA cohort
- Median time to relapse was significantly longer for the Oral-AZA cohort compared with the NoMaint cohort, which is consistent with prolonged median RFS reported in the QUAZAR study (10.2 months Oral-AZA vs 4.8 months placebo, respectively; *P* < 0.001)[4]
- This real-world study suggests that a "watch-and-wait" strategy incurs greater HCRU and costs than an Oral-AZA maintenance therapy regimen
  - These findings add to those from the QUAZAR trial which demonstrated the superior clinical benefit of Oral-AZA maintenance treatment,[4] and reinforce the value of Oral-AZA in the management of patients with AML

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5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed September 11, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
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