HSD97

Real-World Treatment Patterns Among Patients With Relapsed or Refractory (R/R) *NPM1*-Mutated (*NPM1*m) Acute Myeloid Leukemia (AML) in the United States

Grace Gahlon,[1] Shailja Vaghela,[2] Lorena Lopez-Gonzalez,[3] Craig W. Freyer,[3] Shelby Corman,[1] Huan Huang[3]

[1]Precision AQ, Bethesda, MD, USA; [2]HealthEcon Consulting Inc., Ancaster, ON, Canada; [3]Syndax Pharmaceuticals, Inc., New York, NY, USA.

INTRODUCTION

- Nucleophosmin 1 mutations (*NPM1*m) occur in ~30% of adult acute myeloid leukemia (AML) cases[1]
- Approximately 50% of patients with *NPM1*m AML relapse or are refractory (R/R) following initial therapy[2,3]
- There is limited literature on treatment patterns in R/R *NPM1*m AML

OBJECTIVE

- To describe real-world treatment patterns among patients with R/R *NPM1*m AML in the United States

METHODS

Study design and data source

- A retrospective study was conducted using real-world data from COTA Healthcare (COTA)
  - COTA collects electronic health record (EHR) data from ~200 partnered academic and community health care provider sites in the United States
  - The dataset includes patients ≥18 years of age at diagnosis who had a recorded date of diagnosis and clinician notes available in the EHR

Study population

- Adults with an initial AML diagnosis between January 2009 and June 2024 and documented R/R and *NPM1*m status were considered for inclusion (**Figure 1**)
- Patients with R/R *NPM1*m AML, defined as inadequate response, persistent disease/no response, or progression/relapse at any time after initial AML diagnosis as reported in the COTA database, were followed from the date of R/R until death, loss to follow-up, or end of the study period, whichever came first

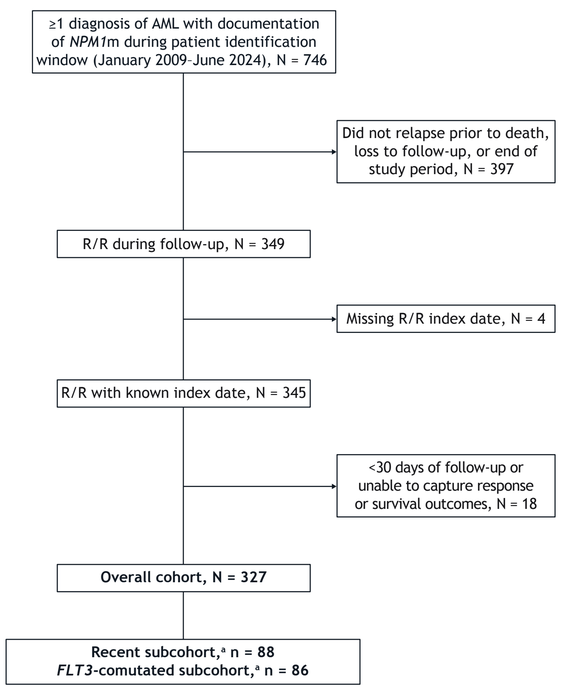
Outcomes and analyses

- Descriptive analyses were performed for the overall cohort and 2 non-mutually exclusive subcohorts to examine treatment patterns after the US Food and Drug Administration (FDA) approval of venetoclax and midostaurin for AML
  - **Overall cohort:** all patients with R/R *NPM1*m AML
  - **Recent subcohort:** patients diagnosed between January 2019 and June 2024 (period following FDA approval of venetoclax in combination with hypomethylating agents for newly diagnosed AML)
  - ***FLT3*-comutated subcohort:** patients diagnosed between January 2017 and June 2024 (includes months immediately before and years following FDA approval of first FLT3 inhibitor [FLT3i], midostaurin, in combination with intensive chemotherapy [IC] for newly diagnosed AML on April 28, 2017) with *NPM1*m AML and an *FLT3* internal tandem duplication (ITD) or *FLT3* tyrosine kinase domain comutation
- In the R/R setting, all treatments, including hematopoietic stem cell transplant (HSCT), administered after first R/R and between subsequent relapse events were grouped into salvage lines
- Salvage regimens were classified into the following hierarchical categories:
  - IC, as defined in 2024 National Comprehensive Cancer Network (NCCN) guidelines[4] (eg, high-dose cytarabine [HiDAC], fludarabine + cytarabine + granulocyte colony-stimulating factor ± idarubicin [FLAG±IDA], mitoxantrone + etoposide + cytarabine [MEC])
  - Low-intensity therapy (LIT), as defined in NCCN guidelines[4] (eg, containing hypomethylating agents, low-dose cytarabine, venetoclax, other targeted therapies)
  - Unknown-intensity therapy, including regimens containing cytarabine with unknown doses and no other therapy categorized as LIT above
  - Investigational agents only

RESULTS

- A total of 327 patients with R/R *NPM1*m AML were included in the **overall cohort** (**Figure 1**, **Table 1**), and ~26% represent the **recent** and ***FLT3*-comutated subcohorts**, respectively

Figure 1. Patient selection from COTA Healthcare database



[a]Recent and *FLT3*-comutated subcohorts were not mutually exclusive.
AML, acute myeloid leukemia; *NPM1*m, nucleophosmin 1 mutated; R/R, relapsed/refractory.

Table 1. Demographic and baseline characteristics[a]

	Overall cohort (initial AML diagnosis: 2009-2024) N = 327	Recent subcohort (initial AML diagnosis: 2019-2024) n = 88	*FLT3*-comutated subcohort (initial AML diagnosis: 2017-2024) n = 86
Age at initial AML diagnosis (y), median (IQR)	62.0 (51.0-70.0)	64.5 (53.8-70.0)	64.0 (52.8-69.0)
19-59, n (%)	141 (43.1)	32 (36.4)	31 (36.0)
≥60, n (%)	186 (56.9)	56 (63.6)	55 (64.0)
Female, n (%)	184 (56.3)	54 (61.4)	47 (54.7)
Race, n (%)			
White	258 (78.9)	64 (72.7)	70 (81.4)
Black or African American	21 (6.4)	5 (5.7)	6 (7.0)
Asian	12 (3.7)	5 (5.7)	5 (5.8)
Other/multiple/missing	36 (11.0)	14 (15.9)	5 (5.8)
Ethnicity, n (%)			
Non-Hispanic	256 (78.3)	69 (78.4)	68 (79.1)
Hispanic, Latino, or Spanish origin	55 (16.8)	17 (19.3)	17 (19.8)
Missing	16 (4.9)	2 (2.3)	1 (1.2)
Clinical practice setting, n (%)			
Academic	192 (58.7)	57 (64.8)	56 (65.1)
Community	135 (41.3)	31 (35.2)	30 (34.9)
Presence of comutations, n (%)			
FLT3-ITD	156 (47.7)	45 (51.1)	79 (91.9)
DNMT3A	107 (32.7)	37 (42.0)	40 (46.5)
IDH2	59 (18.0)	20 (22.7)	16 (18.6)
IDH1	56 (17.1)	15 (17.0)	14 (16.3)
FLT3-TKD	55 (16.8)	13 (14.8)	21 (24.4)
NRAS	38 (11.6)	14 (15.9)	10 (11.6)
Duration of first response, n (%)[b]			
≤6 mo	63 (28.8)	20 (31.3)	21 (39.6)
6-12 mo	68 (31.1)	26 (40.6)	19 (35.8)
≥12 mo	88 (40.2)	18 (28.1)	13 (24.5)
Received HSCT prior to R/R, n (%)	33 (10.1)	11 (12.5)	15 (17.4)
Time from initial AML diagnosis to first R/R (mo), median (IQR)	9.0 (2.7-15.5)	7.1 (2.4-12.8)	5.0 (1.4-10.5)
Duration of follow-up after first R/R (mo), median (IQR)	10.8 (4.0-31.5)	7.8 (3.7-19.6)	7.9 (3.5-19.5)

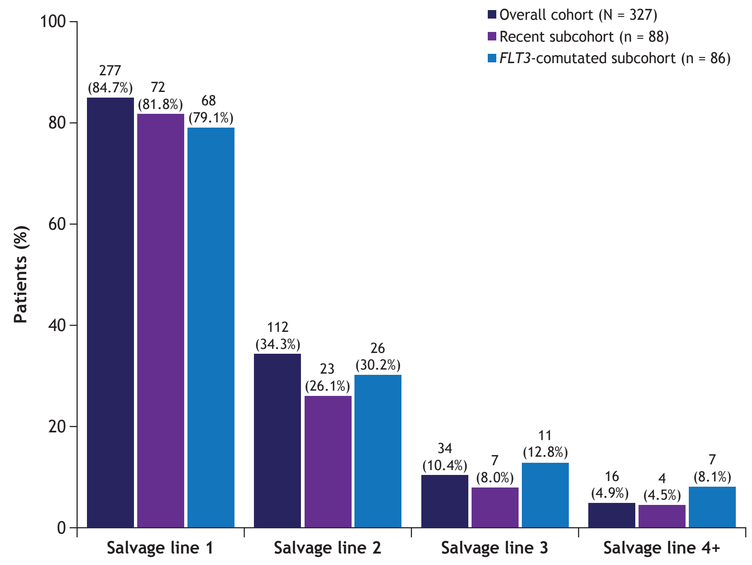
[a]Demographic and baseline characteristics were described at initial AML diagnosis.[b]Among those with composite complete response in frontline (overall cohort, n = 219; recent subcohort, n = 64; *FLT3*-comutated subcohort, n = 53).
AML, acute myeloid leukemia; HSCT, hematopoietic stem cell transplant; IQR, interquartile range; ITD, internal tandem duplication; R/R, relapsed/refractory; TKD, tyrosine kinase domain.

Treatment patterns

Overall cohort

- Forty-nine (15.0%) patients did not receive salvage treatment during follow-up, of whom 39 (79.6%) died prior to end of follow-up, with median time to death of 21 days (**Figure 2**)
- Following the first R/R, 50.8%, 23.9%, 5.5%, and 4.9% of patients received 1, 2, 3, and 4+ salvage lines, respectively (data not shown)
- IC use was highest in salvage lines 1 (51.6%) and 4+ (56.3%; **Figure 3A**, starburst chart)
  - Among IC recipients (all salvage lines), IC only (48.6%-90.9%) was the most common regimen (**Figure 3A**, right table)
  - Among those who received IC (all salvage lines, n = 160), the most frequently used regimens were FLAG (12.9%), HiDAC (10.0%), and MEC (6.9%; data not shown)
- LIT use was highest in salvage line 2 (47.3%) and lowest in salvage 3 (41.2%; **Figure 3A**, starburst chart)
  - No clear utilization trend by salvage line was observed among LIT recipients (**Figure 3A**, left table)
  - Among those who received LIT (all salvage lines, n = 135), the most frequently used regimens were decitabine monotherapy (19.3%), azacitidine monotherapy (12.6%), and decitabine + venetoclax (10.4%; data not shown)
- Use of investigational agent-only regimens was highest in salvage line 4+ (25.0%) and lowest in salvage line 1 (10.1%; **Figure 3A**, starburst chart)
- 37.3% of patients received ≥1 HSCT in the R/R setting, of which 82.0% were transplanted in salvage line 1 and 13.9% in salvage line 2 (data not shown)

Figure 2. Percentage of patients who received regimens by salvage line[a]



[a]Numbers above each bar indicate number and percentage of patients who received any medication regimen in the corresponding line of treatment.

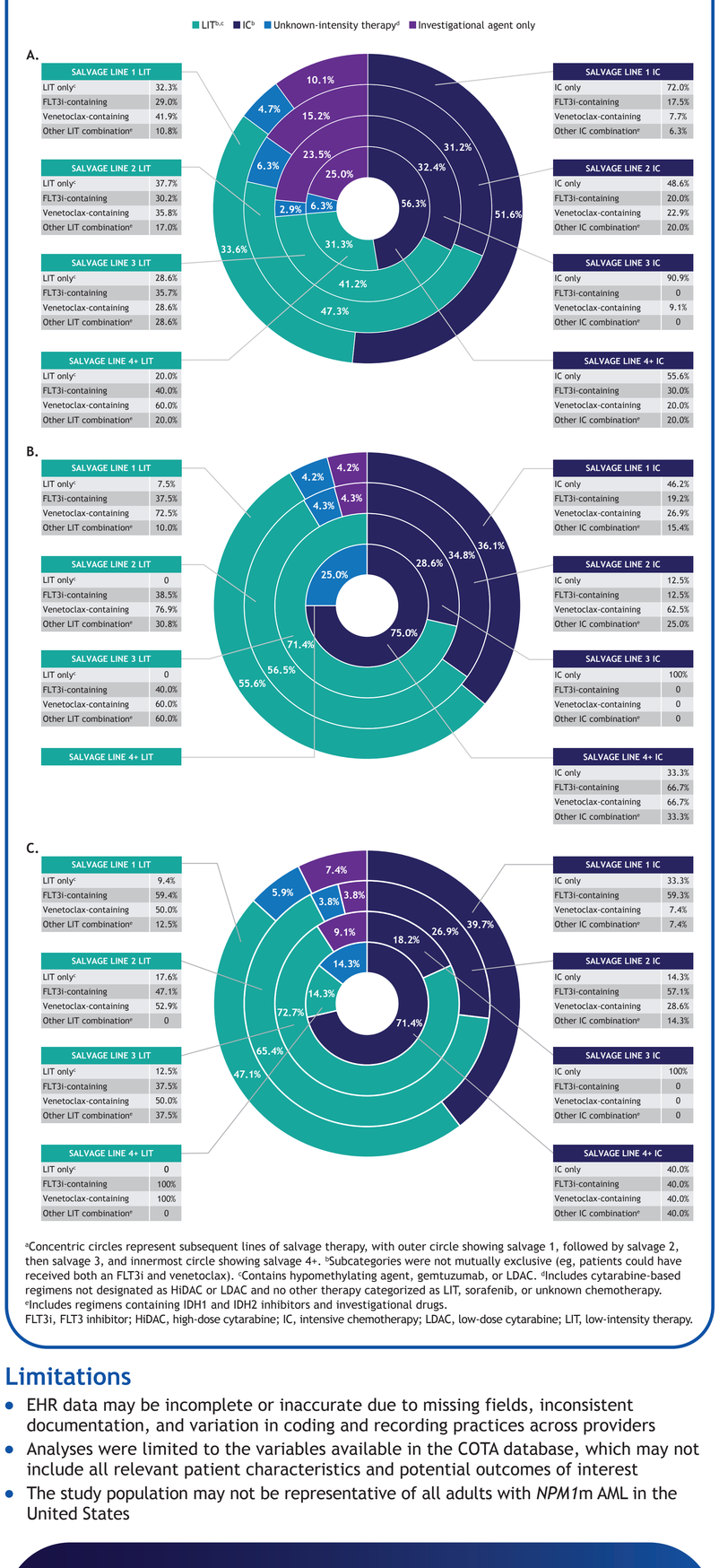
Recent subcohort (diagnosed between January 2019 and June 2024)

- 81.8% of patients received ≥1 salvage therapy (**Figure 2**), and 18.2% did not receive salvage treatment during follow-up (data not shown)
- Use of LIT was higher (55.6%-71.4%) compared with the **overall cohort** (**Figure 3B**, starburst chart)
  - Venetoclax-containing regimens were most common in salvage lines 1 to 3, followed by FLT3i-containing regimens (**Figure 3B**, left table)
  - Among those who received LIT (n = 49), the most frequently used regimens across all salvage lines were decitabine + venetoclax (14.3%), gilteritinib (14.3%), and azacitidine + venetoclax (12.2%; data not shown)
- Use of IC (n = 32) was lower (28.6%-75.0%) when compared with the **overall cohort** for salvage lines 1 to 3 (**Figure 3B**, starburst chart and right table)
  - The most frequently used regimens were FLAG (9.4%), CPX-351 (6.3%), and cytarabine + daunorubicin (6.3%; data not shown)
- Rates of HSCT were similar to the **overall cohort**; 38.9% of patients received ≥1 HSCT in the R/R setting, typically in salvage line 1 (33.3%; data not shown)

FLT3-comutated subcohort (diagnosed between January 2017 and June 2024)

- 79.1% of patients received ≥1 salvage therapy (**Figure 2**), and 20.9% did not receive salvage treatment during follow-up (data not shown)
- 61.8% of patients received FLT3i during any salvage line, of whom 29 (65.9%) received FLT3i with LIT and 19 (63.3%) received FLT3i with IC (data not shown)
- Rates of HSCT were lower compared with the **overall cohort** and **recent subcohort**; 27.9% of patients received ≥1 HSCT in the R/R setting, typically in salvage line 1 (26.5%; data not shown)

Figure 3. Medication regimens by salvage line[a] in the (A) overall cohort (N = 327), (B) recent subcohort (n = 88), and (C) *FLT3*-comutated subcohort (n = 86)



[a]Concentric circles represent subsequent lines of salvage therapy, with outer circle showing salvage 1, followed by salvage 2, then salvage 3, and innermost circle showing salvage 4+. [b]Subcategories were not mutually exclusive (eg, patients could have received both an FLT3i and venetoclax). [c]Contains hypomethylating agent, gemtuzumab, or LDAC. [d]Includes cytarabine-based regimens not designated as HiDAC or LDAC and no other therapy categorized as LIT, sorafenib, or unknown chemotherapy. [e]Includes regimens containing IDH1 and IDH2 inhibitors and investigational drugs.
FLT3i, FLT3 inhibitor; HiDAC, high-dose cytarabine; IC, intensive chemotherapy; LDAC, low-dose cytarabine; LIT, low-intensity therapy.

Limitations

- EHR data may be incomplete or inaccurate due to missing fields, inconsistent documentation, and variation in coding and recording practices across providers
- Analyses were limited to the variables available in the COTA database, which may not include all relevant patient characteristics and potential outcomes of interest
- The study population may not be representative of all adults with *NPM1*m AML in the United States

CONCLUSIONS

- Approximately 1 out of 5 patients in the recent and *FLT3*-comutated subcohorts, respectively, did not initiate any AML treatment following first R/R, mostly due to death
  - This demonstrates a high unmet need for safe and effective salvage therapies, including novel targeted agents, for R/R *NPM1*m AML
- Among patients treated at each subsequent salvage line, treatment patterns in the recent subcohort suggest decreasing use of IC and increasing use of LIT compared with the broader time period included in the overall cohort, likely driven by the availability of venetoclax
- No consistent standard of care was observed for adults with R/R *NPM1*m AML; lack of uniformity across lines of therapy may be attributed to factors such as comutations and numerous drugs in development
- Further research is recommended to understand the considerations for treatment decisions, including reasons for selection of low- versus high-intensity regimens and targeted therapies

REFERENCES

1. Papaemmanuil E, et al. *N Engl J Med*. 2016;374(23):2209-2221.
2. Döhner K, et al. *Blood*. 2005;106(12):3740-3746.
3. Issa GC, et al. *Blood Adv*. 2023;7(6):933-942.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Acute Myeloid Leukemia Version 2.2026. Accessed 8 October 2025. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

ACKNOWLEDGMENTS

We thank Adan Sosa, PharmD, an employee of Syndax Pharmaceuticals, Inc., for their critical review of the data. Editorial and graphic support were provided by Lumanity Communications Inc. and funded by Syndax Pharmaceuticals, Inc.

DISCLOSURES

GG and **SC** are employees of Precision AQ, which received funding from Syndax Pharmaceuticals, Inc. to conduct this study. **SV** is an employee of HealthEcon Consulting Inc. **LL-G**, **CWF**, and **HH** are employees of Syndax Pharmaceuticals, Inc. and may hold shares and/or stock options in the company.

POSTER PRESENTED AT THE INTERNATIONAL SOCIETY FOR PHARMACOECONOMICS AND OUTCOMES RESEARCH (ISPOR) EUROPE CONFERENCE; 9-12 NOVEMBER 2025; GLASGOW, SCOTLAND, UK.