Poster AML 308

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Real-world (RW) outcomes with venetoclax (VEN) in patients with acute myeloid leukemia (AML) from COTA, a US RW evidence database

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Introduction

- A large portion of patients diagnosed with acute myeloid leukemia (AML) are ineligible for intensive chemotherapy due to their advanced age or comorbidities[1,2]
  - These patients have limited treatment options and poor prognosis
- VEN is a selective, small-molecule BCL-2 inhibitor. In a Phase III study of VEN + the hypomethylating HMA azacitidine in previously untreated patients with AML who were ineligible for intensive chemotherapy, limited responses were reported[2]
  - Median duration of complete remission of 17.5 months and median overall survival of 14.7 months
- In November 2018, VEN + HMA or low-dose cytarabine was initially approved for the treatment of patients with AML who are ≥75 years or ineligible for intensive chemotherapy[3]
- This poster presents patient-level curated electronic health record data from centers across the US, in the COTA AML database, to understand the use, safety, and efficacy of VEN in clinical practice

Methods

- This is a retrospective, descriptive analysis of deidentified secondary data from the COTA AML database in the US
- Data were abstracted for adults (≥18 years old) diagnosed with AML who initiated 1L treatment on or after 01/01/2018 and received ≥1 VEN treatment at any point
  - AML diagnosis was based on the World Health Organization's International Statistical Classification of Diseases and Related Health Problems (ICD)-9 code, ICD-10 code, and diagnosis method
  - Patients were excluded if they had concurrent primary malignancies or no date of diagnosis in the electronic health record
- Follow-up was until the last recorded event (last visit or death). The study period for this analysis was 01/2018 to 09/2022. Study endpoints are listed in **Table 1**

Table 1. Study endpoints[a]

Primary	Secondary
Summary statistics of demographics and clinical characteristics, overall and by subgroup	Type and frequency of adverse events with VEN treatment
Summary of treatments received prior to VEN treatment	Median time from VEN treatment initiation to treatment discontinuation
Median VEN treatment duration	Median OS from date of AML diagnosis
	Proportion of patients achieving a real-world response to VEN treatment, by type of response

[a] Table 1 includes a subset of primary and secondary endpoints.

Results

Baseline characteristics

- Of 3836 patients with AML in the database, 1163 patients meeting the inclusion criteria initiated 1L treatment in or after 2018; of these, 636 received ≥1 VEN treatment at any point (**Figure 1**)
- Of patients who received VEN, 47% (299/636) received 1L VEN, and 42% (269/636) received VEN + HMAs in any line
- For patients with treatment prior to VEN (pretreated), 249/337 (74%) were previously treated with chemotherapy
  - For patients treated prior to VEN, other prior treatments were HMA, targeted therapy, investigational drug, chemotherapy + targeted therapy, and HMA + targeted therapy

Figure 1. Attrition and subgroups of patients from the COTA database



- 1L patients were more often treated in community centers than pretreated patients (73% vs 56%), had more comorbidities (56% vs 40%), and had more *TP53* positivity (19% vs 10%) at baseline (**Table 2**)
- Genetic/molecular data were limited
  - Of the most frequently tested mutations, the most common were TP53 (129/461, 28%), RUNX1 (109/444, 25%), TET2 (101/414, 24%), ASLX1 (92/417, 22%), and DNMT3A (91/424, 22%)

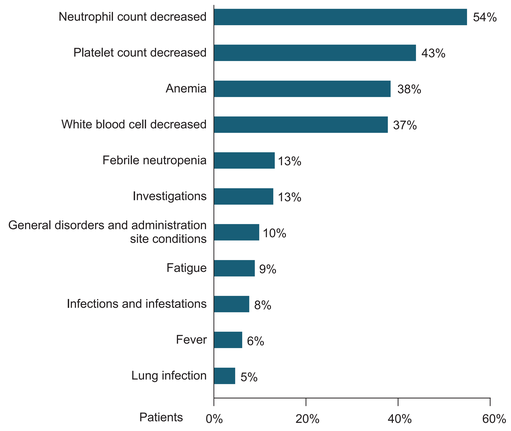
Table 2. Baseline demographic data of all patients treated with VEN

Characteristic	All patients, N=3836	Patients treated with VEN		
		Overall, n=636	Newly diagnosed, n=299	Pretreated, n=337
Male, n (%)	2045 (53)	347 (55)	170 (57)	177 (53)
Age at diagnosis, y, median (Q1-Q3)	65 (52-74)	71 (62-78)	75 (70-81)	66 (55-74)
Comorbidity, n (%)	1439 (38)	303 (48)	167 (56)	136 (40)
AML type, n (%)				
De novo	1459 (38)	209 (33)	83 (28)	126 (37)
Secondary	1176 (31)	234 (37)	124 (42)	110 (33)
Not specified	1201 (31)	193 (30)	92 (31)	101 (30)
Health care provider, n (%)				
Academic	1895 (49)	153 (24)	61 (20)	92 (27)
Academic/community	72 (2)	10 (2)	5 (2)	5 (2)
Community	1550 (40)	407 (64)	217 (73)	190 (56)
Unknown	319 (8)	66 (10)	16 (5)	50 (15)
Treatment status, n (%)				
Newly diagnosed AML	-	299 (47)	299 (100)	-
Pretreated AML	-	337 (53)	-	337 (100)
ECOG PS at diagnosis, n (%)				
0	399 (10)	60 (9)	18 (6)	42 (13)
1	534 (14)	74 (12)	31 (10)	43 (13)
2	169 (4)	25 (4)	9 (3)	16 (5)
3	42 (1)	7 (1)	4 (1)	3 (1)
4	7 (0.2)	0	0	0
Missing	2685 (70)	470 (74)	237 (79)	233 (69)
TP53 positive	-	-	56 (19)	34 (10)

Safety

- Of the 636 patients treated with VEN, 329 (52%) reported at least one adverse event (**Figure 2**)
  - The most common adverse events included decreases in neutrophils (54%), decreases in platelets (43%), and anemia (38%)
- Reliability of the safety data coming from the real-world database should be considered as they may have missing information or inaccurate categorization

Figure 2. Adverse events in ≥5% of all patients treated with VEN



- Toxicity was the main cause of dose reduction and discontinuation
- Dose reduction was reported in 29% of patients treated with VEN
- 53% (338/636) of patients treated with VEN discontinued VEN, with a median time to discontinuation of 49.5 days (**Table 3**)

Table 3. VEN treatment duration and discontinuation

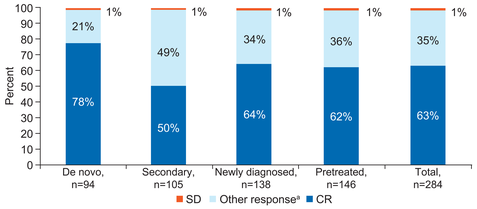
	AML type		Treatment status		
	De novo, n=209	Secondary, n=234	Newly diagnosed, n=299	Pretreated, n=337	Total, n=636
Treatment duration					
Duration of VEN treatment, days, median (Q1-Q3) [min-max]	85 (32-163) [4-857]	77 (30-173) [1-976]	94 (35-213) [1-976]	65 (31-134) [1-870]	78 (32-163) [1-976]
Discontinuation					
Proportion of patients who discontinued VEN, n (%)	109 (52)	134 (57)	162 (54)	176 (52)	338 (53)
Time to VEN discontinuation[a], days, median (Q1-Q3) [min-max]	48 (22-113) [3-518]	50 (24-117) [1-736]	61 (28-126) [1-736]	41 (22-93) [1-870]	50 (24-113) [1-870]

[a]Only includes patients with a documented "discontinuation" in the electronic health record; does not include patients who completed their treatment regimens as planned.

Effectiveness

- Of 284 patients treated with VEN with available response data, 180 (63%) had a complete response (**Figure 3**)

Figure 3. Real-world treatment response in patients treated with VEN



Responses are based on clinician-stated responses from electronic health records and classified by the COTA database. Note that the responses include patients undergoing transplant.
[a] Other response = near CR, very good partial response, partial response, and mixed response. Patients with missing AML type are excluded.

- In subpopulation analyses, the median overall survival was longer in patients with de novo AML compared with secondary AML (**Figure 4**) and in patients with pretreated AML compared with newly diagnosed patients (**Figure 5**)

Figure 4. Overall survival of AML patients treated with VEN by AML type from the date of AML diagnosis

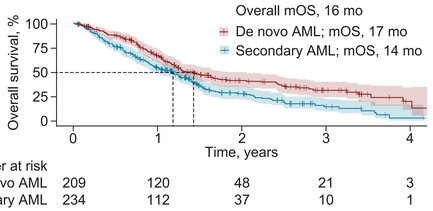
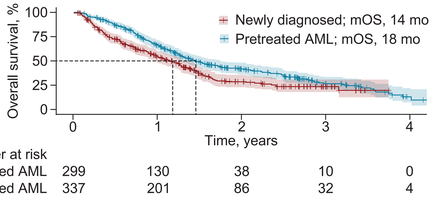


Figure 5. Overall survival of AML patients treated with VEN by treatment status from the date of AML diagnosis



Conclusions

- This study provides an overview of the real-world use of VEN in patients with AML in the US since its approval in November 2018 (patients were mainly treated in community versus academic centers)
- Despite collecting data starting in January 2018 before VEN was approved in November 2018, almost half of patients with AML who initiated treatment after 2018 received 1L VEN
- The real-world CR rate in patients treated with VEN with available data was 63%, but over half of patients treated with VEN discontinued VEN, with discontinuation occurring at a median of 49.5 days
- The real-world median overall survival of patients who received VEN was longer in patients with de novo AML compared with secondary AML and in patients with pretreated AML compared with newly diagnosed AML

Limitations

- As a retrospective study analyzing data from a database, this study is limited by physician-stated outcomes and the potential for incomplete data, imprecise dates, and inaccurate patient censoring
- There is an inherent immortal time bias in overall survival of the pretreated population because the analysis is based on diagnosis date. Pretreated patients have "additional months" before starting VEN compared to the newly treated patients

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Abbreviations

1L, 1st line; AML, acute myeloid leukemia; CR, complete response; ECOG, Eastern Cooperative Oncology Group; HMA, hypomethylating agent; mOS; median overall survival; OS, overall survival; PS, performance status; RW, real-world; SD, stable disease; VEN, venetoclax.

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