AML-119

The Impact of Post-Remission Granulocyte Colony-Stimulating Factor Use in the Phase 3 Studies of Venetoclax Combination Treatments in Patients With Newly Diagnosed Acute Myeloid Leukemia

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OBJECTIVES

To evaluate outcomes by post-remission granulocyte colony-stimulating factor use among patients who received venetoclax-based therapy in the randomized Phase 3 VIALE-A and VIALE-C studies of venetoclax in newly diagnosed acute myeloid leukemia

CONCLUSIONS

In the VIALE-A and VIALE-C studies, granulocyte colony-stimulating factor (G-CSF) was administered post-remission to 49% and 43% of patients who received venetoclax (Ven), respectively; baseline characteristics were similar between patients who received G-CSF and those who did not

Post-remission G-CSF use was safe and was not associated with inferior duration of response or overall survival among Ven-treated patients. Durations of Grade ≥3 neutropenia and febrile neutropenia were generally lower in patients who received post-remission G-CSF

Preferred In VIALE-A and VIALE-C, G-CSF was used per institutional practice. Although the studies were not designed to evaluate the impact of G-CSF on cytopenia management, this post hoc analysis supports the use of G-CSF to manage cytopenias in patients with AML who receive Ven-based therapy in addition to recommended dose modifications

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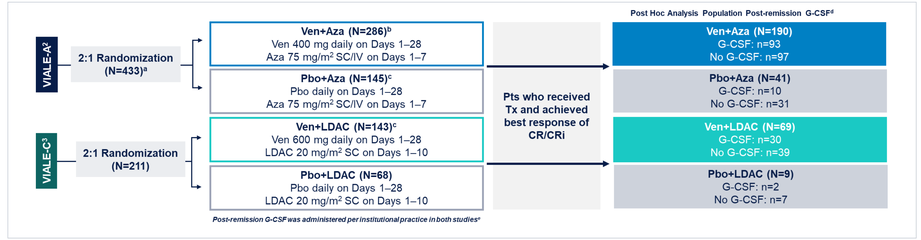
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BACKGROUND

- Patients with acute myeloid leukemia (AML) who are older or ineligible for intensive chemotherapy (IC) have poor outcomes[1]
- Venetoclax (Ven)-based therapy has demonstrated improved outcomes vs low-intensity chemotherapy in patients with newly diagnosed AML ineligible for IC in two randomized Phase 3 trials
  - In VIALE-A (NCT02993523), Ven + azacitidine (Aza) significantly improved median overall survival (OS) vs placebo (Pbo) + Aza (14.7 mo vs 9.6 mo; *P*<.001), as well as the rate of complete remission/complete remission with incomplete hematologic recovery (CR/CRi; 66.4% vs 28.3%; *P*<.001)[2]
  - In VIALE-C (NCT03069352), after an additional 6-mo follow-up from the primary analysis, median OS was improved with Ven + low-dose cytarabine (LDAC) vs Pbo + LDAC (8.4 mo vs 4.1 mo; descriptive *P*=.040), as was the rate of CR/CRi (48.3% vs 13.2%)[3,4]
- In both VIALE-A and VIALE-C, cytopenia with Ven-based therapy was successfully managed with protocol-recommended dose modifications[5,6]
  - Granulocyte colony-stimulating factor (G-CSF) usage was allowed per institutional practice in both studies
- There is limited evidence on the use of granulocyte colony-stimulating factor for cytopenia management and its impact on outcomes in patients with AML who are ineligible for IC

METHODS



[a]2 patients were not stratified by cytogenetic risk and were excluded from the efficacy analysis but included in the safety analysis. [b]3 patients did not receive Tx. [c]1 patient did not receive Tx. [d]Additional data, including for patients who received Pbo, are presented in the supplement. [e]G-CSF product types included filgrastim, lenograstim, pegfilgrastim, lipegfilgrastim, and unspecified. AML, acute myeloid leukemia; Aza, azacitidine; CR, complete remission; CRi, complete remission with incomplete count recovery; G-CSF, granulocyte colony-stimulating factor; IV, intravenously; LDAC, low-dose cytarabine; Pbo, placebo; pt, patient; SC, subcutaneously; Tx, treatment; Ven, venetoclax.

RESULTS

Baseline Characteristics

- In VIALE-A, 190/286 patients (66%) treated with Ven+Aza achieved CR/CRi; 49% received G-CSF after achieving remission
- In VIALE-C, 69/143 patients (48%) treated with Ven+LDAC achieved CR/CRi; 43% received G-CSF after achieving remission
- Baseline Grade ≥3 neutropenia was similar between patients who went on to receive G-CSF and those who did not

Characteristic	VIALE-A		VIALE-C	
	Ven+Aza G-CSF (n=93)	Ven+Aza No G-CSF (n=97)	Ven+LDAC G-CSF (n=30)	Ven+LDAC No G-CSF (n=39)
Median age (range), years	76 (62–90)	77 (53–89)	74.5 (36–92)	76 (68–89)
Female, n (%)	43 (46)	35 (36)	15 (50)	19 (49)
ECOG PS, n (%)				
0–1	52 (56)	56 (58)	17 (57)	23 (59)
2–3	41 (44)	41 (42)	13 (43)	16 (41)
Cytogenetic risk, n (%)[a]				
Intermediate	70 (75)	65 (67)	25 (83)	26 (67)
Poor	23 (25)	32 (33)	2 (7)	11 (28)
Type of AML				
De novo	72 (77)	70 (72)	16 (53)	31 (79)
Secondary	21 (23)	27 (28)	14 (47)	8 (21)
Baseline Gr ≥3 cytopenia, n (%)				
Neutropenia	75 (81)	74 (76)	26 (87)	29 (74)
Thrombocytopenia	38 (41)	49 (51)	20 (67)	18 (46)
Anemia	31 (33)	24 (25)	7 (23)	9 (23)

[a]One patient in the Ven+LDAC G-CSF group had favorable cytogenetics; cytogenetic risk data were missing for 3 patients in the Ven+LDAC G-CSF group and 1 patient in the Ven+LDAC no G-CSF group. AML, acute myeloid leukemia; Aza, azacitidine; ECOG PS, Eastern Cooperative Oncology Group performance status; G-CSF, granulocyte colony-stimulating factor; Gr, grade; LDAC, low-dose cytarabine; Ven, venetoclax.

Post-Remission G-CSF Use and Neutrophil Count Recovery

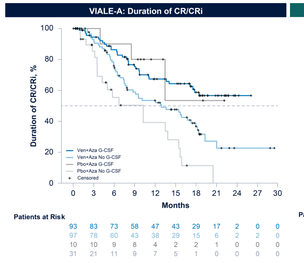
- Among Ven-treated patients who received post-remission G-CSF, the median time to first G-CSF use after remission was 36 days (VIALE-A) and 30 days (VIALE-C)
- For VIALE-A, the median time to neutrophil count recovery from first post-remission Grade 4 neutropenia was 13.5 days (with G-CSF)[a] and 14 days (no G-CSF)[b]; including neutropenia onset pre-remission, the median values were 27 days (with G-CSF)[c] and 31 days (no G-CSF)[c]
- For VIALE-C, the median time to neutrophil count recovery from first post-remission Grade 4 neutropenia was 13 days (with G-CSF)[d] and12.5 days (no G-CSF)[e]; including neutropenia onset pre-remission, the median values were 26 days (with G-CSF)[f] and 27 days (no G-CSF)[g]

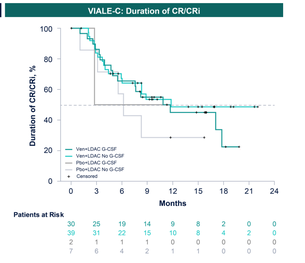
Parameter	VIALE-A	VIALE-C
	Ven+Aza G-CSF (n=93)	Ven+LDAC G-CSF (n=30)
Median number of post-remission G-CSF cycles (range)	3.5 (1–20)	2 (1–10)
Median time from remission to first G-CSF use, days (range)	36 (2–483)	30 (2–459)
Median ANC at initiation of G-CSF use (range), 10^9/L[h]		
All post-remission G-CSF use	0.30 (0–24)[i]	0.42 (0–3.74)[j]
First post-remission G-CSF use	0.20 (0–4.00)[k]	0.48 (0–1.50)[l]
Median ANC at stop of G-CSF use (range), 10^9/L[h]		
All post-remission G-CSF use	1.06 (0–24.34)[m]	0.80 (0.02–35.24)[n]
First post-remission G-CSF use	1.40 (0.04–11.67)[o]	1.39 (0.06–20.70)[p]

[a]Data from 82 patients. [b]Data from 80 patients. [c]Data from 92 patients. [d]Data from 21 patients. [e]Data from 28 pts. [f]Data from 27 patients. [g]Data from 37 patients. [h]Valid ANC from assessments on or within a 3-day window prior to G-CSF initiation or cessation. [i]Data from 276 uses of G-CSF. [j]Data from 79 uses of G-CSF. [k]Data from 65 patients with valid ANC. [l]Data from 22 patients with valid ANC. [m]Data from 295 uses of G-CSF. [n]Data from 72 uses of G-CSF. [o]Data from 57 patients with valid ANC. [p]Data from 21 patients with valid ANC. ANC, absolute neutrophil count; Aza, azacitidine; G-CSF, granulocyte colony-stimulating factor; LDAC, low-dose cytarabine; Ven, venetoclax.

Duration of CR/CRi

- The use of G-CSF after CR/CRi was not associated with inferior duration of CR/CRi in the treatment arms of VIALE-A and VIALE-C



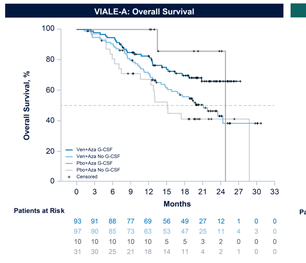


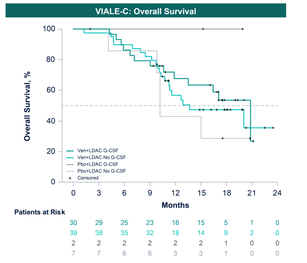
Duration of CR/CRi	VIALE-A		VIALE-C	
	Ven+Aza G-CSF (n=93)	Ven+Aza No G-CSF (n=97)	Ven+LDAC G-CSF (n=30)	Ven+LDAC No G-CSF (n=39)
Median (95% CI), mo	NR (17.5–NR)	12.9 (7.9–17.3)	10.8 (4.9–17.8)	11.8 (5.9–NR)
12-mo rate (95% CI), %	67 (56–76)	53 (42–64)	45 (25–63)	49 (30–65)
18-mo rate (95% CI), %	59 (46–69)	37 (25–48)	23 (5–48)	49 (30–65)
24-mo rate (95% CI), %	57 (44–67)	23 (11–37)	NA	NA

Aza, azacitidine; CR, complete remission; CRi, complete remission with incomplete count recovery; G-CSF, granulocyte colony-stimulating factor; LDAC, low-dose cytarabine; NA, not available; NR, not reached; Pbo, placebo.

Overall Survival

- Post-remission G-CSF use was not associated with inferior OS among Ven-treated patients in VIALE-A and VIALE-C



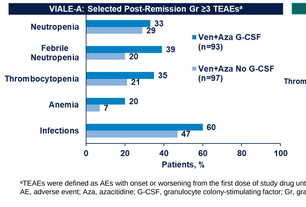


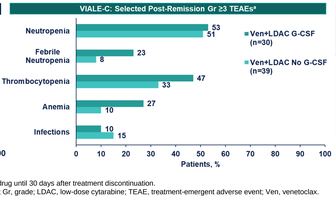
Overall Survival	VIALE-A		VIALE-C	
	Ven+Aza G-CSF (n=93)	Ven+Aza No G-CSF (n=97)	Ven+LDAC G-CSF (n=30)	Ven+LDAC No G-CSF (n=39)
Median (95% CI), mo	NR (NR–NR)	21.1 (15.2–NR)	20.8 (11.9–NR)	13.7 (10.8–NR)
12-mo rate (95% CI), %	83 (73–89)	71 (60–79)	68 (47–82)	57 (39–71)
18-mo rate (95% CI), %	70 (59–78)	56 (44–65)	54 (32–71)	47 (30–63)
24-mo rate (95% CI), %	66 (54–75)	43 (31–55)	NA	NA

Aza, azacitidine; G-CSF, granulocyte colony-stimulating factor; LDAC, low-dose cytarabine; NA, not available; NR, not reached; Pbo, placebo.

Safety

- In both studies, duration of post-remission Grade ≥3 neutropenia or febrile neutropenia was generally shorter with G-CSF use than without G-CSF use





Duration of Post-Remission Neutropenia	VIALE-A		VIALE-C	
	Ven+Aza G-CSF (n=93)	Ven+Aza No G-CSF (n=97)	Ven+LDAC G-CSF (n=30)	Ven+LDAC No G-CSF (n=39)
Median duration of post-remission Gr ≥3 neutropenia (range), days	12.5 (1–696)	16 (1–648)	15 (2–419)	12.5 (5–367)
Median duration of post-remission Gr ≥3 febrile neutropenia (range), days	8 (1–320)	10.5 (2–22)	6 (3–411)	29 (1–30)

[a]TEAEs were defined as AEs with onset or worsening from the first dose of study drug until 30 days after treatment discontinuation.
AE, adverse event; Aza, azacitidine; G-CSF, granulocyte colony-stimulating factor; Gr, grade; LDAC, low-dose cytarabine; TEAE, treatment-emergent adverse event; Ven, venetoclax.