Abstract: P521

Title: FINDINGS FROM AN ANALYSIS OF PATIENTS WITH MONOCYTIC AND MONOCYTIC-LIKE ACUTE MYELOID LEUKEMIA (AML), INCLUDING AML-M4 AND AML-M5, TREATED WITH VENETOCLAX (VEN) PLUS AZACITIDINE (AZA)

Abstract Type: Poster Presentation

Session Title: Acute myeloid leukemia - Clinical

Background:

Ven+Aza has shown efficacy in patients (pts) with AML ineligible for intensive chemotherapy (IC). In monocytic AML (mAML), ex vivo studies have shown that Ven may have reduced activity secondary to overexpression of *MCL1* (Kuusanmaki, 2020; Kurtz, 2022) and clinical studies have suggested that M5 AML may be less sensitive to Ven+Aza (Pei, 2020).

Aims:

To report findings by AML differentiation status using French-American British (FAB) subtyping (M4, M5) and gene expression profiling (GEP) to define mAML from a post hoc analysis of Ven+ Aza in pts with IC ineligible mAML.

Methods:

Pts from the Phase 1b M14-358 (NCT02203773) and Phase 3 VIALE-A (NCT02993523) studies who received Ven+Aza were included. Two methods were used to define mAML: investigator-assessed FAB subtyping (M4, M5, non-M4/M5; n=197) or baseline GEP in pts with >30% AML blasts (n=153); 77 pts had both FAB and GEP data. For GEP, expression levels of genes associated with monocytic differentiation (CD14, ITGAM [CD11b], CD300e, and CR1 [CD35]) were used to classify pts as mAML (high) or non-mAML (low). Complete remission (CR)+CR with incomplete marrow recovery (CRi) rates and median overall survival (mOS) are reported.

Results:

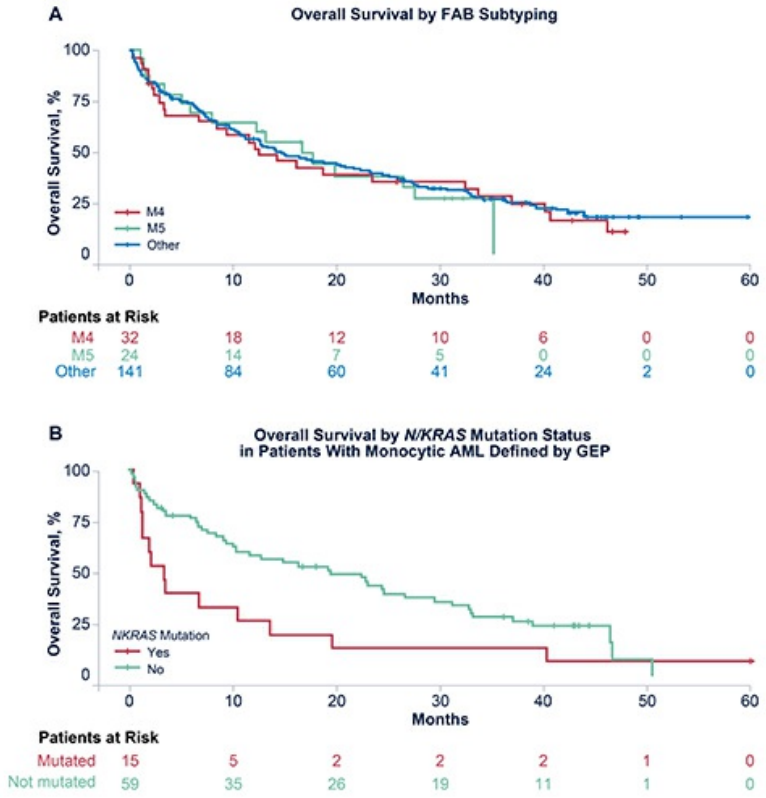
Per FAB subtyping, 32, 24, and 141 pts had M4, M5, or non-M4/M5 AML, respectively. CR+CRi rates per FAB were 63% (95% CI, 45.2−77.1) for M4, 58% (38.8-75.5) for M5, and 71% (62.9-77.8) for non-M4/M5 AML. mOS was 12.4 mo (95% CI, 3.4-32.5), 16.8 mo (5.8-27.5), and 14.7 mo (10.7-22.3), respectively (**Fig. A**). Mutation analysis was performed for 24 pts with M4, 13 pts with M5, and 108 pts with non-M4/M5 AML; *NPM1*^{mut} rates were 13%, 31%, and 14%, *IDH1/2*^{mut} rates were 13%, 38%, and 30%, *TP53*^{mut} rates were 25%, 0%, and 29%, and *N/KRAS*^{mut} rates were 33%, 31%, and 11%, respectively.

Using GEP, 76 and 77 pts were categorized as mAML or non-mAML, respectively. Among FAB evaluable, 86% (6/7) with M5 and 85% (11/13) with M4 were identified as mAML. CR+CRi rates based on GEP were similar between mAML (62% [95% CI, 50.6-71.9]) vs non-mAML (69% [57.8-78.1]), as was mOS (14.7 mo [95% CI, 8.2-24.3] vs 15.2 mo [10.6-20.5]). In mAML vs non-mAML, *NPM1*^{mut} rates were 15% vs 24%, *IDH1/2*^{mut} rates were 27% vs 45%, *TP53*^{mut} rates were 14% vs 15%, and *N/KRAS*^{mut} rates were 20% vs 11%, respectively.

In the mAML group by GEP, 11 pts had *NPM1*^{mut} and 63 pts had wild-type (WT) *NPM1*. CR+CRi rates (95% CI) were 64% (35.4-84.8) vs 60% (48-71.5) and mOS (95% CI) was 46.3 mo (3.4-not reached [NR]) vs 11.5 mo (6.7-22.3) for those with vs without *NPM1*^{mut} mAML, respectively. In pts with *N/KRAS*^{mut} (n=15) vs WT *N/KRAS* (n=59) mAML, CR+CRi rates (95% CI) were 33% (15.2-58.3) vs 68% (55.1-78.3) and mOS (95% CI) was 3.4 mo (1.1-10.4) vs 19.4 mo (9.3-29.2), respectively (**Fig. B**). In the non-mAML group, 18 pts had *NPM1*^{mut} and 56 pts had WT *NPM1*; CR+CRi rates (95% CI) were 72% (49.1-87.5) and 66% (53.0-77.1), respectively, and mOS (95% CI) was 12.5 mo (6.3-NE) and 14.1 mo (8.5-19.9), respectively. In pts with *N/KRAS*^{mut} (n=8) vs WT *N/KRAS* (n=66) non-mAML, CR+CRi rates (95% CI) were 75% (40.9-92.8) vs 67% (54.7-76.8), and mOS (95% CI) was 13 mo (0-27.5) vs 14 mo (10-21), respectively.

Summary/Conclusion:

Outcomes between pts with M4 or M5 AML vs non-M4/M5 AML, as well as mAML vs non-mAML, were overall similar. Differences in response and survival among patients with mAML was most closely linked to the presence or absence of prognostically relevant mutations, such as *NPM1* and *N/KRAS* mutations.



Keywords: Venetoclax, Acute myeloid leukemia, Genomics, Azacitidine