Abstract: S310

Title: VENETOCLAX PLUS AZACITIDINE DELAYS DETERIORATION OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ACUTE MYELOID LEUKEMIA: VIALE-A LONG-TERM FOLLOW UP

Abstract Type: Oral Presentation

Session Title: Quality of life and health economics

Background:

Patients (pts) with acute myeloid leukemia (AML) experience reduced health-related quality of life (HRQoL), including reduced physical (PF) and emotional (EF) function. Many AML treatments, even less aggressive therapies, may be associated with negative impacts on HRQoL, such as high transfusion needs and hospitalization. Objective measurements of HRQoL are important when evaluating the long-term benefits of AML treatments.

Aims:

To characterize HRQoL, particularly delay in deterioration, of pts with AML receiving venetoclax (VEN)+azacitidine (AZA) or placebo (PBO)+AZA in the long-term follow-up (LTFU) of Phase 3 trial, VIALE-A (NCT02993523).

Methods:

Treatment-naïve adults ineligible for intensive chemotherapy were randomized 2:1 to receive VEN+AZA or PBO+AZA. Pt-reported outcomes (PRO) included: EORTC QLQ-C30 global health status (GHS/QoL), PF and EF subscales; PROMIS Cancer Fatigue Short Form 7a (fatigue); and EQ-5D-5L health status visual analog scale (EQ-5D-VAS). PRO data were collected on Day 1 of Cycle 1 and all subsequent cycles. Time to deterioration (TTD) was calculated as the number of days from baseline to the first documented worsening (from baseline) of ≥1 pre-established PRO-specific meaningful clinical threshold (MCT). PRO improvements from baseline of ≥1 PRO-specific MCT were also assessed. Pre-established MCTs for deterioration were a reduction of ≥10 for GHS/QoL, PF, and EF, of 7 for EQ-5D-VAS or an increase of 5 for fatigue. Association between patient characteristics and PROs was assessed, and the within-group level of change in each score was expressed as a standardized effect size (SES) and magnitude of responsiveness (absolute change: SES=0 ~0.19 none; SES=0.20~0.49 small; SES=0.50-0.79 moderate; SES ≥0.8 large).

Results:

VIALE-A LTFU included 431 pts, aged 76 years, median LTFU of 43.2 months. Table 1 shows that the LTFU analysis identified extended TTD for all PROs for patients treated with VEN+AZA, that was significantly longer in the VEN+AZA vs PBO+AZA group for EF, PF, and EQ-5D-VAS. Pts treated with VEN+AZA (vs PBO+AZA) consistently had at least numerically longer TTD across most PROs in key subgroups, including age <75 years, ECOG score >2, achievement of complete response (CR) or CR with incomplete blood cell recovery (CR+CRi), measurable residual disease (MRD) negativity, and post-baseline transfusion independence (TI). Several clinical factors were associated with PRO improvement. For PF subscale, pts who achieved CR, CR/CRi, TI, and/or had an ECOG score >2, had SES that were overall moderate (0.5–0.79), with the magnitude of SES tending to increase from cycle 3 to cycle 33. Similar trends were observed for EF, GHS, and fatigue in pts in those same subgroups, while pts who did not achieve CR, CR/CRi, TI, or had an ECOG score <2 tended to have no or small magnitude in SES (generally ranged 0-0.49) indicating small to no PRO improvements. Among those who achieved CR/CRi, those who also achieved MRD negativity tended towards consistently moderate to large SES across PROs, while small to no PRO improvement was observed in those who did not additionally achieve MRD negativity. Patients who achieved CR/CRi early by Cycle 2 achieved HRQoL improvement at earlier cycles.

Table 1. Median Time to Deterioration in Months in Overall Health/QoL, Physical and Emotional Function, and Fatigue

PRO Measure, median (95% CI)	VEN+AZA (n=286)	PBO+AZA (n=145)
EORTC QLQ-C30 GHS/QoL	19.1 (10.19, 27.55)	9.3 (4.67, NE)
EORTC QLC-C30 PF	10.2 (7.30, 16.01)*	6.2 (4.67, 9.47)
EORTC QLC-C30 EF	27.3 (18.71, 33.90)*	15.7 (7.86, 24.89)
PROMIS Fatigue	9.5 (7.30, 19.04)	8.6 (4.18, 15.19)
EQ-5D-5L VAS	10.7 (7.53, 19.04)**	3.9 (2.37, 7.40)
PRO Measure by subgroups, median		
Age <75 years		
EORTC QLQ-C30 GHS/QoL	21.3*	4.7
EORTC QLC-C30 PF	16.0	9.5
EORTC QLC-C30 EF	NE*	18.2
PROMIS Fatigue	19.2*	6.2
EQ-5D-5L VAS	13.4*	3.8
ECOG >2		
EORTC QLQ-C30 GHS/QoL	21.3	7.9
EORTC QLC-C30 PF	12.3*	6.1
EORTC QLC-C30 EF	NE*	11.5
PROMIS Fatigue	12.0	8.6
EQ-5D-5L VAS	12.5*	3.7
CR+CRi		
EORTC QLQ-C30 GHS/QoL	21.3	16.6
EORTC QLC-C30 PF	12.0	18.4
EORTC QLC-C30 EF	27.3	15.7
PROMIS Fatigue	9.9	15.2
EQ-5D-5L VAS	13.1	7.4
Transfusion Independence -RBC		
EORTC QLQ-C30 GHS/QoL	21.6	16.6
EORTC QLC-C30 PF	15.7	14.1
EORTC QLC-C30 EF	31.4	19.4
PROMIS Fatigue	12.0	11.2
EQ-5D-5L VAS	13.1*	6.8
Transfusion Independence -platelet		
EORTC QLQ-C30 GHS/QoL	21.3	11.0
EORTC QLC-C30 PF	15.7	14.1
EORTC QLC-C30 EF	30.6*	19.7
PROMIS Fatigue	10.7	9.2
EQ-5D-5L VAS	12.5*	6.2
MRD Negative		
EORTC QLQ-C30 GHS/QoL	NE	NE
EORTC QLC-C30 PF	14.7	12.8
EORTC QLC-C30 EF	41.5*	9.7
PROMIS Fatigue	12.9	3.7
EQ-5D-5L VAS	13.4*	6.2

*P<0.01. **P<0.001.
AZA, azacitidine; CI, confidence interval; CR+CRi, complete response with incomplete blood cell recovery; EF, emotional functioning; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer quality of life questionnaire; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; GHS, global health status; MRD, measurable residual disease; NE, not estimable; PBO, placebo; PF, physical functioning; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; VAS, visual analog scale; VEN, venetoclax.

Summary/Conclusion: The longer preservation of PROs such as PF, EF, and fatigue, including significantly longer TTD in PF, EF, and EQ-5D-VAS observed with VEN+AZA vs PBO+AZA suggests that VEN positively impacts HRQoL of elderly AML pts. Based on SES analysis, achieving remission and MRD negativity, ECOG score >2, or TI might be associated with improved PF, EF, and fatigue.

Keywords: Acute myeloid leukemia, Venetoclax, Quality of life