Health-related quality of life (HRQoL) with enasidenib versus conventional care regimens in older patients with late-stage mutant-IDH2 relapsed or refractory acute myeloid leukemia (R/R AML).

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Background: Enasidenib (ENA) is an oral inhibitor of mutant-IDH2 (mIDH2) proteins. In the phase 3 IDHENTIFY trial, ENA improved event-free survival (EFS), overall response, and complete remission rate vs conventional care regimens (CCR) ($P < 0.01$ for all) in patients (pts) ≥ 60 years of age with mIDH2 R/R AML with 2 or 3 prior treatments (Tx) (DiNardo 2021). Pt-reported HRQoL was a second- ary trial endpoint. Methods: IDHENTIFY is an open-label, randomized trial (NCT02577406). Pts were preselected to a CCR (SC azacitidine, intermediate- or low-dose Ara-C, or supportive care) and then randomized 1:1 to ENA 100 mg/d or CCR in 28-d cycles. Key HRQoL endpoints were mean changes from baseline (CFB) overall and by clinical response in the Global Health Status/QoL, Physical Func- tioning, Role Functioning, Fatigue, and Dyspnea domains of the EORTC QLQ-C30 questionnaire, and in EQ-5D-5L utility index (UI) and visual analogue scale scores. The QLQ-C30 and EQ-5D-5L were as- sessed on D1 of each Tx cycle (C) and at end of Tx. Minimally important differences (MIDs) in CFB scores within or between Tx arms were based on accepted thresholds. Sensitivity analysis using imput- ed data on CFB was conducted using pattern mixture modeling. Results: HRQoL-evaluable cohorts in- cluded 118/158 (74.7%) pts in the ENA arm and 80/161 (49.7%) in the CCR arm; 40 ENA pts and 81 CCR pts were not evaluable due to missing data at baseline (BL; 22 ENA and 51 CCR) and/or at ≥1 post-BL visit (26 ENA and 69 CCR). Pts ineligible for HRQoL analyses had lower response rates and worse EFS and overall survival than HRQoL-evaluable pts. Overall QLQ-C30 completion rates in the ENA and CCR arms were 79% and 65%, respectively ($P < 0.001$). While there was no meaningful im- provement or worsening from BL (ie, exceeding MID) within either Tx arm in the key QLQ-C30 do- mains, scores worsened during initial Tx cycles and then improved with continued Tx. Mean EQ-5D-5L scores also worsened during early cycles in both Tx arms, with meaningful UI deterioration in the ENA arm from C2 through C7. However, between-group comparisons showed no consistent differences be- tween ENA and CCR in mean CFB. Sensitivity

analysis with imputation of missing CFB data showed worsened HRQoL compared with non-imputed data in the CCR arm but not with ENA. In the ENA arm, clinical responders reported relatively stable mean HRQoL scores over time, and non-responders showed no meaningful differences in CFB vs the CCR arm. Conclusions: HRQoL measures tended to worsen during early cycles in both Tx arms and gradually improved with continued Tx. Data should be interpreted with caution as only approximately one-half of pts in the CCR arm were HRQoL-evaluable. ENA improved clinical efficacy measures vs CCR without compromising HRQoL in older pts with R/R AML. Clinical trial information: NCT02577406. Research Sponsor: Celgene, a Bristol-Myers Squibb Company.