Intrapatient comparative analysis of zanubrutinib plus obinutuzumab efficacy in relapsed/refractory (R/R) follicular lymphoma (FL) using the growth modulation index (GMI)

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ABSTRACT

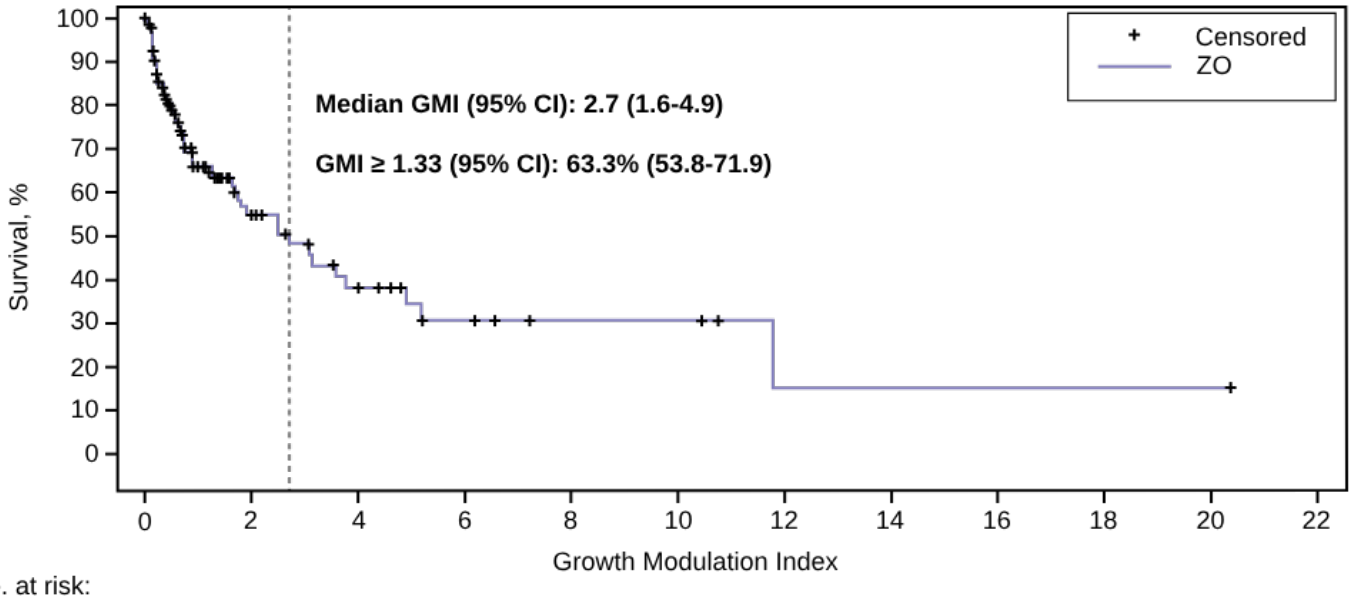
Background: In ROSEWOOD (NCT03332017), a global, randomized, open-label, phase 2 study, median PFS in patients (pts) with R/R FL was significantly longer with zanubrutinib + obinutuzumab (ZO) vs obinutuzumab (O) alone and compared favorably with the PFS with their last prior treatment. To overcome limitations of cross-study comparisons, the GMI uses each pt as their own control to evaluate tx efficacy by comparing PFS with each successive tx (GMI >1, present tx extends PFS vs prior tx; GMI ≥1.33, significant clinical activity). ZO efficacy was analyzed in the tx sequence received by ROSEWOOD pts using an intra-pt comparison analysis with the GMI clinical endpoint.

Methods: PFS was assessed by independent central review; ROSEWOOD censoring rules were used. GMI was defined as (PFS_n from ZO or O)/(PFS_{n-1} from last prior line) with the distribution estimated by the Kaplan-Meier (KM) method. The 95% CIs were estimated using the Brookmeyer and Crowley method (median GMI) and Greenwood's formula with logit transformation (proportion within each interval).

Results: In ROSEWOOD, pts were randomized to ZO (n=145) or O (n=72); 5 pts in the ZO arm and 3 in the O arm were excluded from the analysis (PFS_{n-1} data unavailable). KM curve analysis confirmed prior observations that median PFS with ZO, but not O, was longer than with the last tx (ZO, 28.0 vs 12.1; O, 10.4 vs 11.5 months), the most frequent of which were rituximab-containing regimens (ZO, 69%; O, 60%) and immunochemotherapy (ZO, 54%; O, 51%). In the overall population, median GMI for ZO and O, respectively, was 2.7 (95%CI, 1.6-4.9; Figure) and 0.9 (95%CI, 0.5-1.7). With ZO, 63.3% (95%CI, 53.8-71.9) of pts had a GMI ≥1.33 and 34.1% (95%CI, 25.9-43.3) had a GMI <1. In a subgroup analysis, pts in the ZO arm with 2 prior lines (n=63) had a median GMI of 2.5 (95%CI, 0.9-NE); 65.6% (95%CI, 50.8-77.8) of pts had a GMI ≥1.33. Pts in the ZO arm with >2 prior lines (n=77) had a median GMI of 3.1 (95%CI, 1.3-4.9); 61.8% (95%CI, 49.2-73.0) of pts had a GMI ≥1.33.

Conclusions: Post hoc GMI analysis of ROSEWOOD efficacy data showed that the majority (>60%) of pts with R/R FL who received ZO had a significant (GMI ≥1.33) improvement in PFS vs their last prior tx, regardless of the number of prior tx. The median GMI of 2.7 in the overall population was more than double the 1.33 threshold for meaningful clinical activity compared with the last prior tx. These data further support the benefit of ZO as a novel tx for R/R FL.

Figure. KM Analysis of GMI in the ZO Arm



No. at risk:

Zanubrutinib	140	30	15	7	4	4	1	1	1	1	1	0