Zanubrutinib + obinutuzumab vs last prior treatment in R/R follicular lymphoma: growth modulation index from ROSEWOOD

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ABSTRACT

Background: ROSEWOOD (NCT03332017), a randomized, open-label, phase 2 study, compared the efficacy and safety of zanubrutinib + obinutuzumab (ZO) with obinutuzumab (O) alone in patients (pts) with R/R follicular lymphoma (FL) who had received ≥2 prior lines of systemic therapy. The Growth Modulation Index (GMI) uses each pt as their own control to evaluate efficacy by comparing PFS durations with successive treatments (txs). To analyze the efficacy of ZO in the tx sequence received by pts in ROSEWOOD, we performed an intrapatient comparison analysis using the GMI clinical endpoint.

Methods: PFS was assessed by independent central review. Censoring rules were defined in the study. GMI was defined as (PFS_n with ZO or O)/(PFS_{n-1} with last prior line), with GMI ≥1.33 considered clinically significant. GMI distribution, including median and proportion in each interval, was estimated using the Kaplan-Meier method. The 95% CIs were estimated using the Brookmeyer and Crowley method for median GMI and the Greenwood formula with logit transformation for proportion in each interval.

Results: In ROSEWOOD, 145 pts were randomized to ZO and 72 to O. Five pts were excluded from the GMI analysis in the ZO arm and 3 in the O arm, as no PFS_{n-1} data were available. Analysis confirmed previous observations that median PFS with ZO, but not with O, was longer than that with the last prior tx (ZO, 28.0 vs 12.1; O, 10.4 vs 11.5 mo), the most frequent of which were rituximab-containing regimens (ZO, 69%; O, 60%) and immunochemotherapy (ZO, 54%; O, 51%). Median GMI was 2.7 (95% CI, 1.6-4.9) with ZO and 0.9 (95% CI, 0.5-1.7) with O. In the ZO arm, 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.

Conclusion: Post hoc GMI analysis of ROSEWOOD data showed that >60% of pts with R/R FL receiving ZO had clinically significant improvement in PFS vs last prior tx. These data further support the benefit of ZO as a novel therapeutic option for pts with R/R FL.