**Comparative efficacy of zanubrutinib plus obinutuzumab versus last prior treatment in relapsed/refractory follicular lymphoma: Growth modulation index analysis from ROSEWOOD study**

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**ABSTRACT**

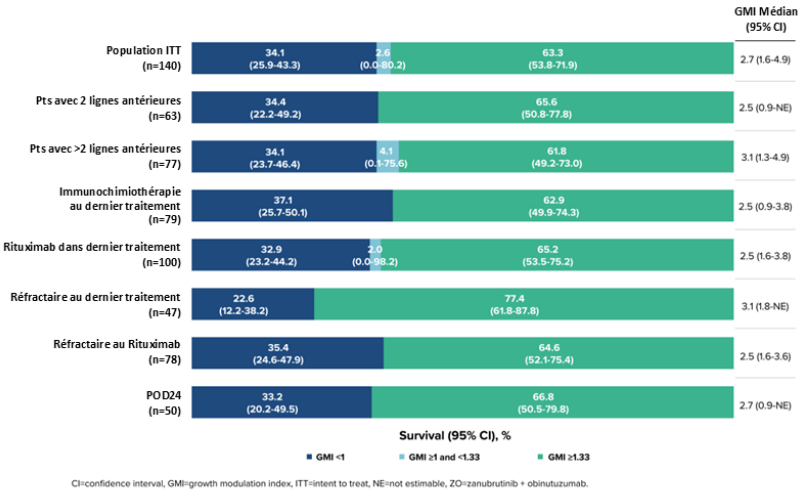
**Introduction:** ROSEWOOD (NCT03332017), a phase 2 study of zanubrutinib + obinutuzumab (ZO) vs obinutuzumab (O) alone in patients (pts) with relapsed/refractory (R/R) follicular lymphoma (FL) with ≥2 prior lines of treatment (tx), showed median PFS was longer with ZO vs O, and PFS compared favorably with the last prior tx (Zinzani et al. JCO; 2023). The Growth Modulation Index (GMI) allows for indirect comparisons across different studies and compares PFS durations with successive txs using each pt as their own control. A GMI ≥1.33 is often used as a threshold for clinical activity. To compare efficacy of ZO in pts in ROSEWOOD vs their last prior tx, a GMI analysis was performed.

**Methods:** GMI was defined as ($PFS_n$ from ZO or O)/($PFS_{n-1}$ from last prior line). Median GMI, GMI distribution, and the proportion within each interval were estimated using the Kaplan-Meier method. The Brookmeyer and Crowley method was used to estimate 95% CIs for median GMI, and the Greenwood formula with logit transformation was used to estimate 95% CIs for the proportion within each interval.

**Results:** In ROSEWOOD, 145 pts were randomized to the ZO arm and 72 to the O arm. Pts with no available $PFS_{n-1}$ data were excluded (ZO, n=5; O, n=3). Analysis confirmed that median PFS with ZO, but not with O, was longer vs the last prior 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%). Overall, median GMI was 2.7 (95% CI, 1.6-4.9) in the ZO arm and 0.9 (95% CI, 0.5-1.7) in the O arm. In the ZO arm, 63.3% (95% CI, 53.8-71.9) of pts had a GMI ≥1.33. Subgroup analyses in the ZO arm showed a median GMI of 2.5 (95% CI, 0.9-NE) in pts with 2 prior lines (n=63) and 3.1 (95% CI, 1.3-4.9) in those with >2 prior lines (n=77); GMI ≥1.33 in 65.6% (95% CI, 50.8-77.8) and 61.8% (95% CI, 49.2-73.0) of pts, respectively. Median GMI was 2.5 (95% CI, 0.9-3.8) in pts who received immunochemotherapy as their last tx and 2.5 (95% CI, 1.6-3.8) in those with rituximab-containing regimens as their last tx; GMI ≥1.33 in 62.9% (95% CI, 49.9-74.3) and 65.2% (95% CI, 53.5-75.2) of pts, respectively. Median GMI =3.1 (95% CI, 1.8-NE) in pts who were refractory to their most recent line of therapy and 2.5 (95% CI, 1.6-3.6) in those refractory to rituximab; GMI ≥1.33 in 77.4% (95% CI, 61.8-87.8) and 64.6% (95% CI, 52.1-75.4) of pts, respectively. In pts with progressive disease ≤24 months after first line tx, median GMI =2.7 (95% CI, 0.9-NE) and 66.8% (95% CI, 50.5-79.8) had a GMI ≥1.33.

**Conclusions:** Most (>60%) pts with R/R FL receiving ZO in ROSEWOOD had a significant (GMI ≥1.33) improvement in PFS vs their last prior tx, irrespective of the number of prior lines and in all tested subgroups of clinical interest. The overall median GMI of 2.7 was more than double the 1.33 threshold for meaningful clinical activity. These data further support the benefit of ZO as a novel therapeutic option for pts with R/R FL.

**Figure 1. Analyse de sous-groupes du GMI dans le bras ZO**




CI=confidence interval, GMI=growth modulation index, ITT=intent to treat, NE=not estimable, ZO=zanubrutinib + obinutuzumab.