Comparison of zanubrutinib (zanu) and acalabrutinib (acala) in B-cell malignancies: an adverse event (AE)-based analysis

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Background: Acala and zanu are 2nd generation Bruton tyrosine kinase inhibitors (BTKis) that have demonstrated improved safety profiles vs 1st generation BTKi ibrutinib in clinical trials. While head-to-head comparison of zanu vs acala is lacking, a recent meta-analysis of clinical trials provided a comprehensive, indirect comparison of the AE profiles in B-cell malignancies (Hwang, *Hemasphere.* 2023;7(S3):1134). This study aims to evaluate costs and impacts on quality of life (QoL) for zanu vs acala using their AE profiles.

Methods: A health economic model was developed to determine cost and QoL associated with AE management for zanu and acala. The incidence rates (*IRs*) of all grade and grade ≥3 AEs of interest (n=21, including bleeding events, hypertension, atrial fibrillation, cytopenias, infections, headache, arthralgia, diarrhea) were taken from the meta-analysis. Additional model inputs, such as disutility, average duration of AE, and unit cost of each AE were sourced from published literature and publicly available cost databases in consultation with clinical experts. The model was developed from the US perspective, considering Medicare costs, inflated to 2023 USD. Model outcomes were AE management cost (=$IR * unit\ cost$) and quality-adjusted life years (QALYs) lost due to AE (=$IR * Disutility * Duration/365.25$).

Results: In the base-case scenario (considering all AEs), treating a hypothetical cohort of 1000 patients (pts) with zanu instead of acala yielded cost savings of $124K and 3.7 QALY gains (i.e., 3.7 years extra in full health). Subgroup analysis for severe (grade ≥3) and non-severe AEs (grade 1-2) demonstrated similar trends. A sensitivity analysis limited to AEs significantly different between zanu and acala (n=13) yielded consistent results. Additionally, a probabilistic sensitivity analysis, conducted with 1000 iterations to account for uncertainty in model parameters, confirmed robustness of the model, indicating stable conclusions across a wide range of parameter uncertainties.

Table 1. Results based on severity of AEs (per 1000 patients)

AEs	Incremental Cost (zanu vs acala)	Incremental QALY (zanu vs acala)
All grade AEs	**-$124,454**	**+3.69**
Grade 1-2	-$69,060	+1.89
Grade ≥ 3	-$55,394	+1.80

Conclusion: This analysis suggested that zanu is cost-saving and associated with added health benefits compared to acala in terms of AE management in pts with B-cell malignancies. Should these results derived from meta-analysis of clinical trial data be applicable to real-world pt populations across different indications, the potential cost savings could be considerable. These results could be further improved if the differences in efficacy of zanu vs acala are also incorporated.