Zanubrutinib vs. Acalabrutinib in B-Cell Malignancies: An Adverse Event-Based Economic Analysis

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Background: B-cell malignancies comprise a heterogenous group of cancers, including B-cell lymphoma, B-cell leukemias, and plasma cell dyscrasias. In clinical trials for B-cell malignancies, the 2nd generation Bruton tyrosine kinase inhibitors (BTKis) zanubrutinib and acalabrutinib had improved safety vs the 1st generation BTKi ibrutinib; however, direct comparison of 2nd generation BTKi is lacking. A recent meta-analysis provided a comprehensive, indirect comparison of the adverse event (AE) profiles of acalabrutinib and zanubrutinib in clinical trials for B-cell malignancies (Hwang et al. *Hemasphere.* 2023;7(S3):1134).

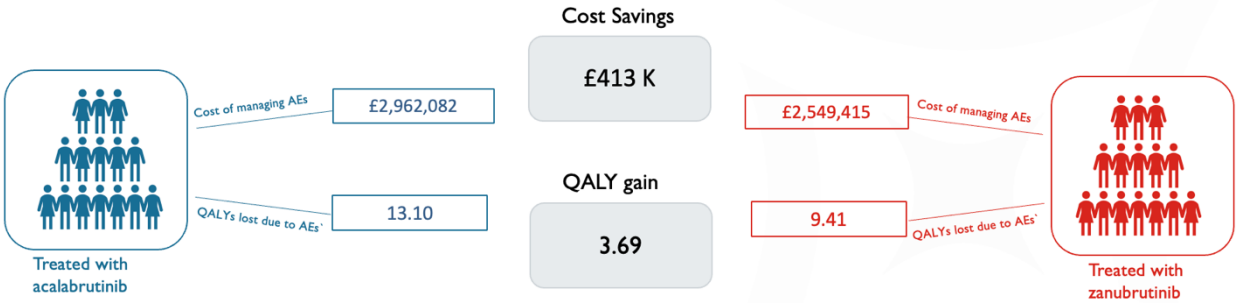
Aims: This study aims to evaluate impacts on costs and quality of life (QoL) for zanubrutinib vs acalabrutinib from the United Kingdom (UK) healthcare perspective using the AE profiles from Hwang et al.

Methods: The cost and QoL associated with AE management for zanubrutinib and acalabrutinib were determined using a health economic model developed from the UK's National Health Service (NHS) perspective. Model inputs included: incidence rates (*IRs*) of all grade and grade ≥3 AEs of interest (n=21; e.g., bleeding events, hypertension, atrial fibrillation, cytopenias, infections, headache, arthralgia, diarrhea), as reported in the meta-analysis; disutility and mean duration of AEs, as reported in published articles and previous single technology appraisals performed by the National Institute of Health and Care Excellence (NICE); and the unit cost of each AE, based on the National Schedule of NHS costs database (FY 2021-22), AE specific Healthcare Resource Group (HRG) codes, and consultation with clinical experts. Unit costs were inflated to 2023 GBP (£). Model outcomes were AE management cost (=$IR * unit\ cost$) and quality-adjusted life years (QALYs) lost due to AEs (=$IR * Disutility * Duration/365.25$). Robustness of the analysis was tested using probabilistic sensitivity analysis (PSA).

Results: In the base case (considering all AEs), treatment of a hypothetical cohort of 1000 patients with zanubrutinib instead of acalabrutinib was associated with cost savings of £413K and 3.69 QALY gains (i.e., 3.69 years extra in full health) (Figure 1). Subgroup analysis for grade ≥3 AEs (£148K cost savings, 1.80 QALY gains) and grade 1-2 AEs (£264K cost savings, 1.89 QALY gains) showed similar trends. A sensitivity analysis limited to AEs significantly different between zanubrutinib and acalabrutinib (n=13) yielded consistent results (£442K cost savings, 3.88 QALY gains). A PSA, conducted with 1000 iterations to account for uncertainty in model parameters, confirmed robustness, indicating stable conclusions across a wide range of parameter uncertainties.

Summary/Conclusion: The results of this economic analysis indicate that zanubrutinib was cost-saving and associated with added health benefits compared to acalabrutinib in terms of AE management in patients with B-cell malignancies in the UK. If these results derived from meta-analysis of clinical trial data could be assumed generalizable to the real-world patients across different indications, the savings could be substantial.

Figure. Results of base case analysis for a hypothetical cohort of 1000 patients



AE, adverse event; QALY, quality-adjusted life years.