Lifetime costs of CLL by first-line treatment selection: continuous monotherapy zanubrutinib versus venetoclax-based regimens

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CURRENT CHARACTER COUNT (including section headers and spaces): (3,979, 4500)

OBJECTIVE: Despite advances in treatment, CLL is associated with long-term clinical management and substantial healthcare resource use, as well as costs borne by patients and their caregivers. Current novel treatment options in CLL include zanubrutinib, a monotherapy Bruton tyrosine kinase inhibitor (BTKi) which is given until disease progression, and venetoclax-based combination regimens which are given as fixed duration treatments. While published indirect treatment comparisons have found that zanubrutinib is associated with long-term clinical benefit versus venetoclax-based fixed duration regimens in treatment-naïve CLL, cost analyses remain uncertain. Venetoclax-based regimens in CLL are often perceived to be less costly because treatment duration is finite, however, drug and administration costs only account for part of the total lifetime cost of a treatment pathway. The objective of this study was to estimate total lifetime costs associated with first-line use of zanubrutinib and approved fixed-duration venetoclax-based regimens over a lifetime horizon.

METHODS: Incremental costs associated with zanubrutinib, venetoclax + obinutuzumab (V+O), ibrutinib + venetoclax (I+V) and acalabrutinib + venetoclax (A+V) were estimated over a lifetime horizon. In order to accurately capture costs, a three-state Markov model (progression-free [PF], progressed disease [PD] and death) was developed with health state transitions informed by time to progression, pre-progression survival and post-progression survival. Time to discontinuation (TTD) estimated the proportion of patients remaining on first line (1L) treatment, while second-line (2L) PFS data were used as a proxy for time on subsequent treatment. TTD for V+O, I+V and A+V assumed treating up to the maximum treatment durations specified in clinical trials. Patients were assumed to receive venetoclax plus rituximab following 1L zanubrutinib, and zanubrutinib following 1L venetoclax-based regimens, using published trial data to inform the duration of treatment (MURANO and ALPINE, respectively). Costs included treatment acquisition and administration costs, additional direct costs (concomitant intravenous immunoglobulin [IVIG], tumour lysis syndrome [TLS] prophylaxis management and adverse event management) as well as indirect costs (productivity loss and travel for patients and caregivers). Given that the use of fixed duration regimens is more prominent in Europe, costs were estimated in Germany, Italy and France. The primary outcome of the analyses was total and incremental costs (both direct and indirect). Sensitivity analyses were conducted to assess the uncertainty in the model results.

RESULTS: Across Germany, Italy and France, total lifetime costs were lowest with zanubrutinib and higher for V+O, I+V and A+V (Germany and Italy only, as A+V is not reimbursed in France). Across all countries, drug costs (both 1L and subsequent treatment) represented the greatest proportion of costs. In Germany, 1L drug costs represented 56%, 21%, 31% and 29% of total lifetime costs for a CLL

treatment strategy starting with zanubrutinib, V+O, I+V and A+V, respectively. 2L drug costs were proportionally lower for zanubrutinib (25%) versus V+O, I+V and A+V (52%, 50% and 53%, respectively); similar patterns were observed for Italy and France. While 1L costs were higher with zanubrutinib, these were offset over the lifetime horizon by lower subsequent treatment costs, lower TLS prophylaxis management costs, lower cost of adverse event management and lower societal costs. Sensitivity and scenario analyses showed results were consistent with the base case.

CONCLUSIONS: This cost analysis found that a 1L treatment strategy starting with zanubrutinib was cost saving compared with venetoclax-based fixed duration regimens for patients with TN CLL in Germany, Italy and France from a societal perspective. These results suggest that drug acquisition costs alone do not fully capture the lifetime economic impact of first-line treatment strategies, underscoring the importance of including all relevant costs when evaluating the total costs of a given treatment pathway.

Financial disclosures: LM, LB and RW are employees of BeOne Medicines. This study was funded by BeOne Medicines.