Background

- Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is an indolent lymphoproliferative disorder characterized by an excessive accumulation of uncontrolled, small, mature-appearing CD5+ B-lymphocytes mainly within peripheral blood, bone marrow, lymph nodes, and secondary lymphoid organs.1

- Bruton's tyrosine kinase inhibitor (BTKi) plays a key role in B-cell receptor signaling. It introduced the paradigm change in the CLL/SLL treatment pathway and has challenged the role of chemo-immunotherapy (CT).2

- A recent update to National Comprehensive Cancer Network (NCCN) clinical guidelines included zanubrutinib, a next-generation BTKi, as preferred treatment for treatment-naive (TN) CLL/SLL.1 The efficacy and safety of zanubrutinib are examined in the randomized, phase 3 SEQUOIA trial (NCT03366333) comparing zanubrutinib plus rituximab (R) to another TN cohort of patients with previously untreated UCLL/SLL and without del 17p mutation.3

- The objective of this study is to develop a budget impact model (BIM) and estimate the incremental costs associated with using zanubrutinib in the population from the US commercial and Medicare perspectives.

Methods

- A Microsoft Excel-based BIM was developed to compare a “reference scenario” reflecting the current market scenario of treatment options (i.e., before zanubrutinib entry), with an “alternative scenario” which also included zanubrutinib for a proportion of patients based on its projected uptake in TN CLL/SLL patients (i.e., after zanubrutinib entry) over a three-year time horizon. (Figure 1)

Table 1. Epidemiology Parameters Used in the BIM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Data</th>
<th>Source</th>
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<tbody>
<tr>
<td>CLL/SLL = Chronic lymphocytic leukemia/small lymphocytic lymphoma; DSA = Drug acquisition and administration; CTC = Clinical trial registry; N = Number of patients; PMPM = per member per month; TN = Treatment-naive</td>
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- The targeted patients are in line with the SEQUOIA trial population and the hypothetical 1,000,000 total plan size was assumed. The number of eligible patients entering the model in each year was estimated based on US-specific epidemiological data.

- A 3% payer perspective (i.e., 80% commercial and 20% Medicare) was used in base case analysis.

- Zanubrutinib was assumed to treat until progression and the treatment duration was informed by the time-to-progression (TTP) extrapolated from the observed data from SEQUOIA cohort 1 data. Treatment duration of other regimens was estimated on the constant hazard ratios derived from a standard NMA analysis or modelled as a fixed duration based on drug labels.4

- Progressed patients are allowed to receive active subsequent treatments, and the costs associated with 2L were calculated as one cost of the model. i.e., venetoclax + rituximab (V+R) was assumed for patients who progressed following BTKi whilst Brutinib + rituximab (B+R) was assumed for patients who progressed following C78023 (TN + R) or other combination regimens. Upon treatment discontinuation, a 4-week treatment-free interval was modelled before patients continue to the next line of treatment, to reflect clinical practice more closely.

- Budget impact and per-member-per-month (PMPM) costs were estimated for the base-case scenarios of clinical practice with and without zanubrutinib. Deterministic sensitivity analyses (DSA) were conducted by varying each input by ±20% to assess parameter uncertainties and explore key model drivers.

Table 2. Treatment Regimens and Cost Inputs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost Category</th>
<th>Cost Input</th>
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</thead>
<tbody>
<tr>
<td>Zanubrutinib</td>
<td>Drug acquisition cost (per cycle)</td>
<td>$10,000</td>
</tr>
<tr>
<td>Obinutuzumab</td>
<td>Drug administration cost (per cycle)</td>
<td>$200</td>
</tr>
</tbody>
</table>

- Model Inputs and Assumptions

- The number of eligible patients entering the model in each year was derived from a hypothetical plan size of 1 million, annual incidence by perspective, and proportion of patients eligible and receiving active 1L treatment (Table 1).

- Modelled treatment options for TN CLL were zanubrutinib, Brutinib, acalabrutinib, obinutuzumab + chlorambucil, rituximab, venetoclax + obinutuzumab, bendamustine + rituximab, chlorambucil + rituximab (Table 2).

- Market share data for the reference scenario were sourced from BeGene market research.4 Zanubrutinib uptake was assumed to be 10% and distributed proportionally to the current treatment mix. The market share for Brutinib 1L was assumed to be constant throughout the time horizon.

- Drug acquisition costs (commercial) were extracted from wholesale acquisition costs (WAC) reported in REDD BOOKD. Average selling prices (ASP) published by the CMS were used to inform Medicare perspectives. Drug wastage was considered for treatments that are dependent on weight or body surface area (BSA), as well as with relative dose intensity adjusted.

- Cost administration costs were assumed B0.0. Chemotherapy administration costs were informed by 2021 Physicians’ Fee & Coding Guide (informal to 2022).11

- Medical resource-use (MRE) costs include those incurred by disease management, treatment monitoring (i.e., one-off prophylaxis treatment of tumor lysis syndrome [TLS] for venetoclax-based regimens), MRU costs per month (e.g., hospitalization, emergency department visit, physician’s office visit, and lab tests) were extracted from Kabadd 2020, a retrospective database analysis for patients without AEs, and inflated to 2022.12 TLS one-off costs were calculated based on risk category as reported in MURANO trial.10

- Adverse event (AE) management costs were applied at the start of each treatment and only grade 3+ AEs that were considered serious, last for patients for at least one treatment were included. AE incidences were extracted from trial publications, and costs per AE were derived from CMS.gov for Medicare and multiplied by a ratio of 2.05 for commercial.12

- Table 3 presents the deterministic sensitivity analysis (DSA) that drug costs, payer perspective and treatment duration had the greatest impact on the budget impact of healthcare costs estimated over a three-year time horizon (Figure 3).

- Market uptake for zanubrutinib was based on BeGene forecasts and may be subject to future updates according to real-world utilization.

- Where treatment options could be defined as a mixed basket of chemotherapy and combination therapies, changes to the default inputs impacted acquisition and administration costs but not efficacy.

- This analysis does not address any potential clinical or QoL benefits that could be associated with the inclusion of zanubrutinib in a healthcare formulary.

Conclusions

The budget impact analysis suggests that providing access to zanubrutinib for patients with TN CLL/SLL is associated with cost savings in a US health plan.

References