BUDGET IMPACT ANALYSIS OF ZANUBRUTINIB FOR THE TREATMENT OF ADULT PATIENTS WITH MANTLE CELL LYMPHOMA WHO HAVE RECEIVED AT LEAST ONE PRIOR THERAPY FROM THE PAYER PERSPECTIVE IN THE UNITED STATES

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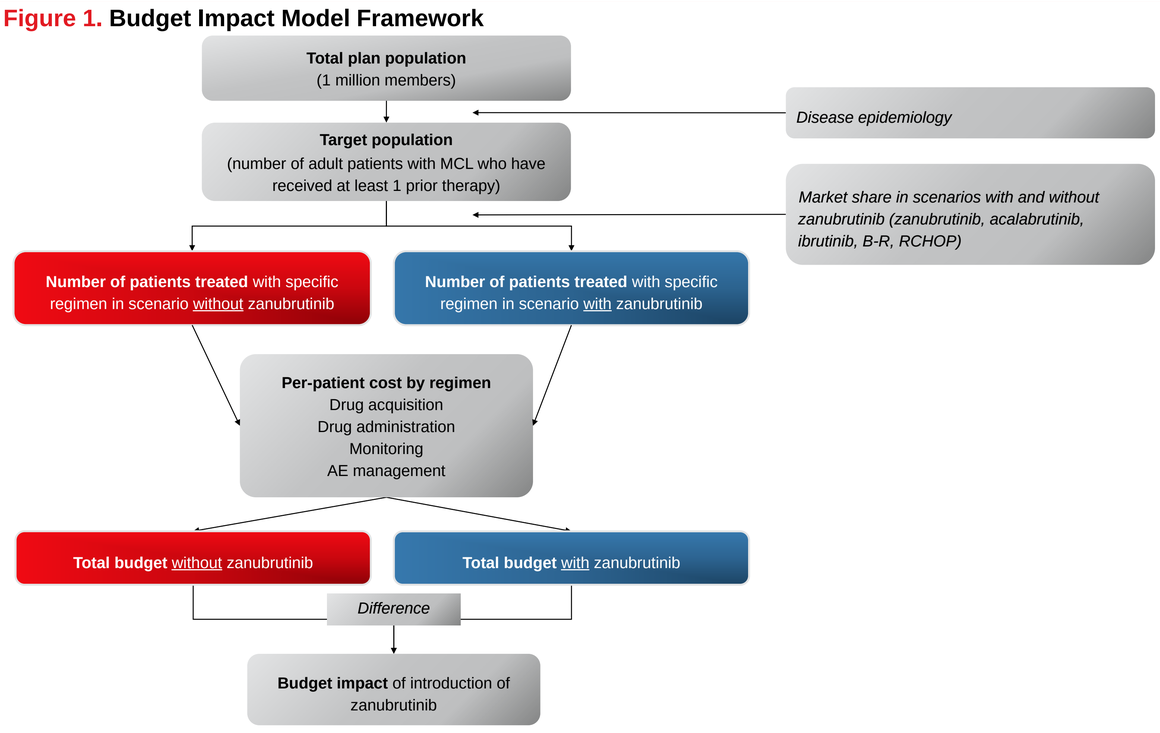
BACKGROUND

- Mantle cell lymphoma (MCL) is a rare, aggressive, B-cell non-Hodgkin lymphoma (NHL) subtype which is estimated to account for approximately 3% of all NHL cases in the United States (US).[1] The incidence is about 1.15 persons per 100,000 in the US[2]
- Treatment options for patients with advanced MCL include induction therapy with chemoimmunotherapy followed by an autologous stem cell transplant and rituximab maintenance therapy. For patients unfit for transplant, a less aggressive chemoimmunotherapy regimen with rituximab maintenance therapy can be used. Most patients with MCL will eventually relapse and require further treatment[3]
- Zanubrutinib, a Bruton's tyrosine kinase inhibitor (BTKi) received accelerated approval by the US Food and Drug Administration in November 2019 for the treatment of adult patients with MCL who have received at least 1 prior therapy[4]
- Bendamustine / rituximab (B-R), rituximab /cyclophosphamide / doxorubicin / vincristine / prednisone (RCHOP), and other BTKi, acalabrutinib and ibrutinib, are commonly used in the US for the treatment of MCL
- The objective of this analysis was to evaluate the budget impact of adding zanubrutinib to the formulary for the treatment of adult patients with MCL who have received at least 1 prior therapy from the US Medicare and commercial payer perspectives

Figure 1. Budget Impact Model Framework



Abbreviations: AE, adverse event; B-R, bendamustine and rituximab; MCL, mantle cell lymphoma; RCHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

METHODS

Model Overview

- The model compared the total costs between two scenarios over one-year time horizon **(Figure 1, Table 1)**:
  - A scenario without zanubrutinib on the formulary: Patients might receive acalabrutinib, ibrutinib, B-R, or RCHOP
  - A scenario with zanubrutinib on the formulary: Patients might receive one of the aforementioned therapies or zanubrutinib
- The analysis was conducted from the US Medicare and commercial payer perspectives, each with 1 million members. Target population was adult patients with MCL who received at least 1 prior therapy, consistent with the approved indication for zanubrutinib[4]
- Costs included drug acquisition, drug administration, monitoring, and adverse event (AE) management. All costs were reported in 2020 US dollars

Table 1. Model Input Category and Reference

Input Category	Reference
Treatment Costs and Duration	• Dosing regimen was based on trial publications or prescribing information for each comparator[4-9] • Median duration of treatment reported in the trial publications or prescribing information was used, with treatment duration capped at 12 months given the 1-year time horizon **(Table 2)** • Drug costs were based on the wholesale acquisition cost (WAC) obtained from the RED BOOK[10]
Monitoring Costs	• Frequency of monitoring or testing was based on prescribing information • Included outpatient visit, complete blood count, electrocardiography, blood electrolyte panel, urinalysis, and renal function test • Unit costs were based on the National Fee Analyzer[11]
AE Management Costs	• AE that were grade 3 or higher and occurred in at least 5% of patients were included: leukopenia, anemia, thrombocytopenia, fatigue, infection • Incidence rates were based on trial publications or prescribing information • Unit cost were obtained from the Healthcare Cost and Utilization Project[12]
Market Share	• Market share was based on market research. A market shift of 4% was assumed from existing BTKi (i.e., acalabrutinib, ibrutinib) to zanubrutinib in the first year after it was added to the formulary[13]

Key Model Assumptions

- Only patients who would be treated with BTKi (i.e., acalabrutinib, ibrutinib) would switch to zanubrutinib
- A proportion of patients on an RCHOP regimen would receive maintenance rituximab following RCHOP
  - Patients receiving rituximab maintenance would incur additional drug acquisition, drug administration, and monitoring costs depending on the treatment duration of maintenance rituximab
  - Any rituximab-related AE would have occurred during administration of the rituximab-containing RCHOP regimen
- Patients on a B-R regimen would not receive maintenance rituximab
- For intravenously administered drugs, single-use vials were used. Wasted drug was accounted for in the drug cost

Model Outputs

- Total budget impact for the entire health plan
- Per-member-per-year (PMPY) and per-member-per-month (PMPM) budget impact
- Per-patient-per-year (PPPY) and per-patient-per-month (PPPM) budget impact

Sensitivity Analysis

- One-way sensitivity analysis was conducted by varying the key variables:
  - Wholesale Acquisition Cost for each individual drug
  - Treatment duration for BTKi
  - Target population size

Table 2. Model Inputs for Drug Dosing, Frequency, Duration of Treatment, and Costs

Regimen	Dose Per Administration (Route)	Number of Doses Per Month	Drug Cost Per Month	Drug Administration Cost Per Month [a]		Treatment Duration, Months	Monitoring Cost Per Month		AE Management Cost (One-Time Total Cost)	
				Medicare	Commercial		Medicare	Commercial	Medicare	Commercial
Zanubrutinib	160 mg (oral) or 320 mg (oral)	60.9 (160 mg) or 30.4 (320 mg)	$13,124	NA	NA	12[b]	$159	$417	$4,376	$4,394
Acalabrutinib	100 mg (oral)	60.9	$14,269	NA	NA	12[c]	$159	$417	$2,446	$2,445
Ibrutinib	560 mg (oral)	30.4	$15,034	NA	NA	12[d]	$159	$417	$3,638	$3,657
B-R	B: 184 mg (IV) R: 766 mg (IV)	B: 2.2 R: 1.1	$18,927	$385	$1,130	5.5[e]	$168	$465	$5,235	$5,598
RCHOP followed by R maint.	RCHOP: R: 766 mg (IV) C: 1532 mg (IV) H: 102 mg (IV) O: 3 mg (IV) P: 100 mg (oral) R maint.: 766 mg (IV)	RCHOP: R: 1.4 C: 1.4 H: 1.4 O: 1.4 P: 7.2 R maint.: 0.5	RCHOP: $12,708 R maint.: $545	RCHOP: $508 R maint.: $71	RCHOP: $1,526 R maint.: $207	12[f]	$168	$465	$17,060	$17,495

Abbreviations: AE, adverse event; B, bendamustine; B-R, bendamustine and rituximab; C, cyclophosphamide; H, doxorubicin; IV, intravenous; maint., maintenance; MCL, mantle cell lymphoma; NA, not applicable; O, vincristine; P, prednisone; R, rituximab; RCHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. [a] National Fee Analyzer costs for *Current Procedural Terminology* codes 96413 and 96417[11] ; [b] Observed median duration in phase 1 and 2 trials combined was 17.5 months[4,5] ; [c] Observed median duration in the clinical trial was 13.8 months[6] ; [d] Observed median duration in the clinical trial was 14.4 months[7] ; [e] Observed duration was not publicly reported[8] ; treatment duration of six 28-day cycles (approximately 5.5 months) was assumed based on the maximum number of cycles per study protocol. [f] RCHOP: 4.1 months, R maintenance: 7.9 months. In the pivotal clinical trial for RCHOP, RCHOP was administered for eight 21-day cycles with an observed median duration of 152 days,[9] but in this model we assumed that patients received 6 cycles, which was a conservative assumption based on more recent clinical trials.[14,15]

RESULTS

Budget Impact

- In a hypothetical Medicare plan with 1 million members, there were 13 eligible R/R MCL patients and adding zanubrutinib to the formulary was associated with a cost saving of $8139 over 1 year ($633 PPPY; $0.001 PMPM) **(Figure 2, Table 3)**
- In a hypothetical commercial plan with 1 million members, there was 1 eligible R/R MCL patient and adding zanubrutinib to the formulary was associated with a cost saving of $739 over 1 year ($633 PPPY; $0.000 PMPM) **(Figure 3, Table 3)**

Figure 2. Budget Impact Results for Medicare Plan (1 Million Members)

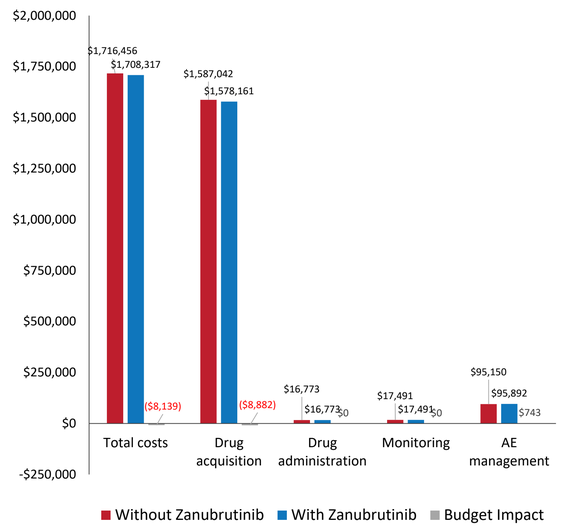
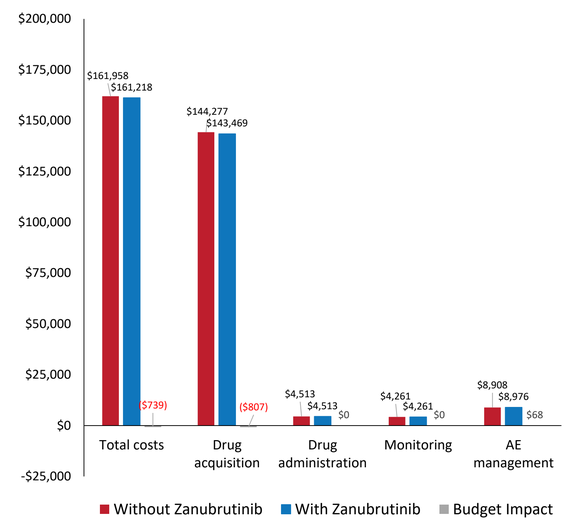


Figure 3. Budget Impact Results for Commercial Plan (1 Million Members)

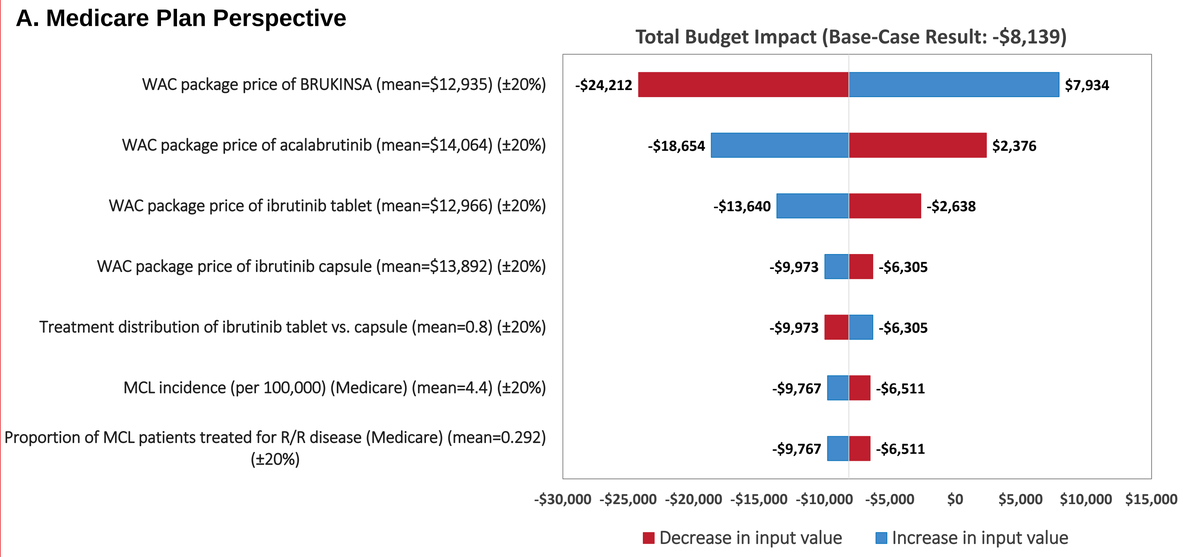


Sensitivity Analysis

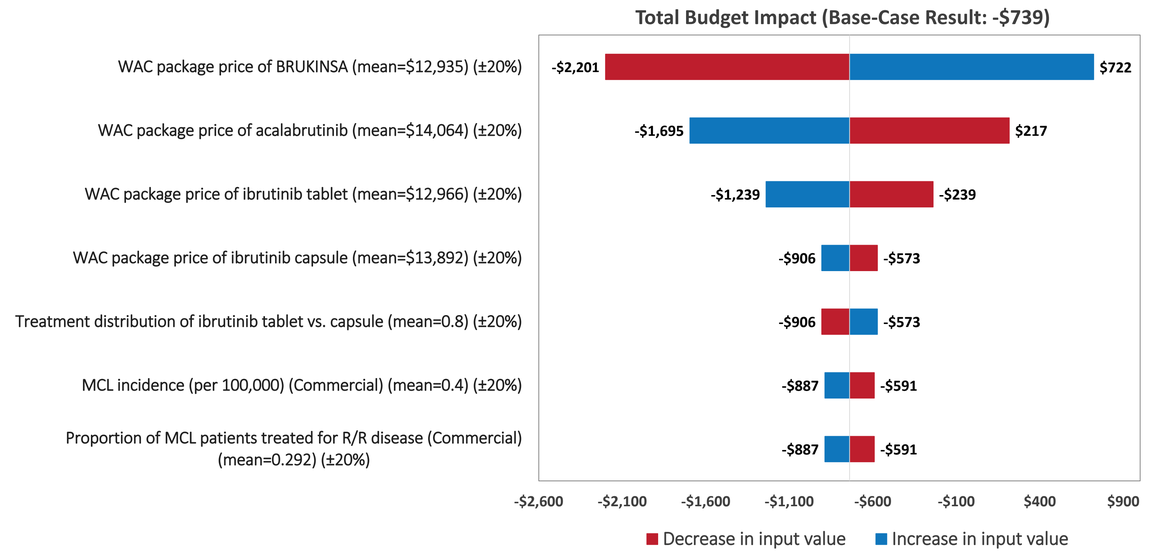
- The 1-year budget impact results were most sensitive to drug acquisition cost of zanubrutinib, followed by drug acquisition cost of the other BTKi (i.e., acalabrutinib, ibrutinib) **(Figure 4)**

Figure 4. One-way Sensitivity Analysis Tornado Diagram for Total Budget Impact

A. Medicare Plan Perspective



B. Commercial Plan Perspective



Abbreviations: MCL, mantle cell lymphoma; R/R, relapsed/refractory; WAC, wholesale acquisition cost.

Table 3. Budget Impact Results

	Budget Impact
Medicare Plan (1 Million Members)	
Total	-$8,139
PMPM	-$0.001
PMPY	-$0.008
PPPM	-$53
PPPY	-$633
Commercial Plan (1 Million Members)	
Total	-$739
PMPM	-$0.000
PMPY	-$0.001
PPPM	-$53
PPPY	-$633

Abbreviations: PMPM, per-member-per-month; PMPY, per-member-per-year; PPPM, per-patient-per-month; PPPY, per-patient-per-year.

LIMITATIONS

- Treatment duration and safety profile data were derived from individual clinical trials for each regimen due to the lack of head-to-head trials between MCL treatment regimens
- There was a lack of clinical trial data for B-R and RCHOP specific to this target population
- The model did not include the costs after disease progression
- The model did not account for medication adherence or persistence

CONCLUSIONS

- Zanubrutinib offers an important treatment option for adult patients with MCL who have received at least 1 prior therapy.
- Adding zanubrutinib to the formulary is associated with cost savings over 1 year, driven primarily by the lower annual per-patient drug acquisition cost of zanubrutinib

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