ZANUBRUTINIB VERSUS IBRUTINIB TO TREAT ADULTS WITH WALDENSTRÖM MACROGLOBULINEMIA: A COST PER RESPONDER MODEL FROM A PAYER PERSPECTIVE IN THE UNITED STATES

Sizhu Liu[1], Keri Yang[1], John Carter[2], Hoa Pham[1], Mark Balk[1], Marjan Massoudi[1], Rongzhe Liu[2], Xin Gao[2], Boxiong Tang[1]

[1]BeiGene USA, San Mateo, CA; [2]OPEN Health, Bethesda

Introduction

- Bruton tyrosine kinase (BTK) inhibition is an effective treatment approach for patients with Waldenström macroglobulinemia (WM)[1]
- The randomized, phase 3 ASPEN study (NCT03053440) compared the efficacy and safety of ibrutinib, a first-generation BTK inhibitor (BTKi), with zanubrutinib, a novel, highly selective BTKi, in patients with WM[2-3]
- On August 31, 2021, the US Food and Drug Administration (FDA) approved zanubrutinib (Brukinsa®) for adult patients with WM[4]

Objective

- To estimate the cost per responder (CPR) for zanubrutinib versus ibrutinib in treatment-naive or relapsed/refractory WM patients from a payer perspective in the United States

Methods

Model structure

- An Excel-based model was developed to estimate the CPR economic impact of zanubrutinib versus ibrutinib in adult patients with WM over a 1-year time horizon

Model inputs

- Clinical response was based on the primary endpoint of the ASPEN trial, very good partial response (VGPR) or complete response (CR) assessed by the independent review committee
- Drug costs were calculated using wholesale acquisition costs (WAC), duration of treatments, and dosing and frequencies from the ASPEN trial or prescribing information **(Table 1)**
  - The WAC costs for zanubrutinib and ibrutinib were obtained from IBM Micromedex RED BOOK Online®[5]
  - Treatment duration was assumed to be 12 months for both arms

Table 1. Key model inputs – drug costs[5,6]

Treatment	Dosage	WAC	Daily cost
Zanubrutinib	160 mg orally twice daily	$13,491	$449.70
Ibrutinib	420 mg orally once daily	$13,926	$497.36

- Probabilities for the following grade ≥3 adverse events (AEs) were extracted from the ASPEN trial and included in the model: atrial fibrillation/flutter, diarrhea, hemorrhage, hypertension, neutropenia, infection, and secondary malignancy **(Table 2)**
  - AE management costs were estimated based on the incidence of BTKi AEs of interest (grade ≥3) from the ASPEN trial and costs per AE as reported by the Healthcare Cost and Utilization Project (HCUP)[7]
  - Cost per AE from HCUP was adjusted to 2021 United States dollars using the medical care component of the Consumer Price Index[6]

Table 2. Key model inputs – AE rates and costs

Adverse event[2-3]	AE Cost	Zanubrutinib	Ibrutinib
Atrial fibrillation/flutter[a]	$10,231	0%	4%
Diarrhea	$8,177	3%	1%
Hemorrhage	$19,441	6%	8%
Hypertension	$3,808	6%	11%
Neutropenia[b]	$14,389	20%	8%
Infection[c]	$6,761	18%	19%
Secondary malignancy[d]	$24,652	2%	1%

a The AE cost was based on atrial fibrillation alone.
b Including neutropenia, neutrophil count decreased, febrile neutropenia, agranulocytosis, neutropenic infection, and neutropenic sepsis.
c Most of these were mucosal infections involving the sinopulmonary (i.e., upper respiratory tract infection, nasopharyngitis, lower respiratory tract infection, respiratory tract infection) and urinary tracts (urinary tract infection). For the analysis, the model uses acute upper respiratory infection for the cost estimation.
d Ultraviolet light-mediated skin cancers (i.e., basal cell carcinoma, squamous cell carcinoma of skin, Bowen disease, skin cancer, malignant melanoma).

Outcome

- As no patient achieved a CR in both arms, cost per responder was calculated as the total cost of one treatment group divided by the proportion of patients who achieved IRC-assessed VGPR in that treatment group

Sensitivity Analysis – Breakeven Analysis

- A breakeven analysis was used to calculate the WAC of ibrutinib where the difference in CPR was equal to zero dollars compared to zanubrutinib

Results

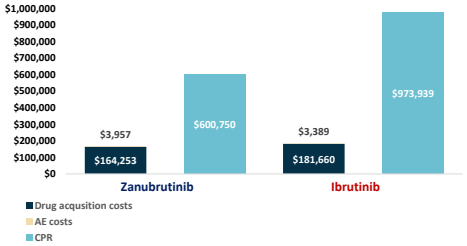
- In modeled ibrutinib patients, the total direct "medical cost per patient" was $185,048 *(drug acquisition: $181,660; AEs: $3,389)* **(Table 3, Figure 1)**
- In modeled zanubrutinib patients, the total direct "medical cost per patient" was $168,210 *(drug acquisition: $164,253; AEs: $3,957)*
- CPR was $973,939 for ibrutinib and $600,750 for zanubrutinib
- Zanubrutinib was associated with lower direct medical costs (-$16,838 per patient) and lower CPR (-$373,189)

Table 3. CPR Model results

	Zanubrutinib	Ibrutinib
Drug acquisition cost	$164,253	$181,660
AE cost	$3,957	$3,389
Total costs	$168,210	$185,048
Responders	28%	19%
Cost per responder (CPR)	**$600,750**	**$973,939**

Abbreviations: AE, adverse event

Figure 1. Summary of total cost and CPR



Conclusion

- In adult patients with treatment-naive or relapsed/refractory WM, zanubrutinib represents a cost-saving option to achieve clinical response, with a lower cost per response compared to ibrutinib from a payer perspective in the United States

- In the breakeven analysis, the WAC for ibrutinib (strength: 420 mg, package size: 28) would have to be reduced by 39% (i.e., $13,926 to $8,437) to yield an equal value of CPR
- Sensitivity analysis indicated that drug acquisition costs and management costs of neutropenia were the most significant drivers of the model

Discussion

- This CPR analysis suggests that over a 1-year time horizon, zanubrutinib was associated with lower direct medical costs and lower CPR in adult WM patients
- Future research is needed with real-world outcomes and a longer follow-up period to substantiate the findings of this analysis

References

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Correspondence: tom.liu@beigene.com

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