EE506

Clinical Outcomes and Associated Costs of Treating Patients With Waldenström Macroglobulinemia in the First-Line Setting With Bruton Tyrosine Kinase Inhibitors

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OBJECTIVE

To evaluate clinical benefits and associated treatment-related costs of first-in-class Bruton tyrosine kinase inhibitor (BTKi) ibrutinib, follow-on BTKi zanubrutinib, and rituximab-based regimens using data from United States prescribing information, clinical trials, and real-world evidence

CONCLUSIONS

Using base case assumptions and conservative clinical efficacy estimates, results suggest clinical benefits and costs are similar for assessed Waldenström macroglobulinemia treatments, exclusive of treatment acquisition costs for ibrutinib and zanubrutinib in the first-line (1L) settings

Scenario analyses examining efficacy using clinical trial data derived from head-to-head trials also support the comparable value of ibrutinib relative to zanubrutinib in the 1L setting, with greater clinical benefits associated with ibrutinib and similar nondrug costs for ibrutinib and zanubrutinib

Adverse event (AE) costs were lower for ibrutinib after accounting for reduced AE costs resulting from potential ibrutinib dose reductions among eligible patients

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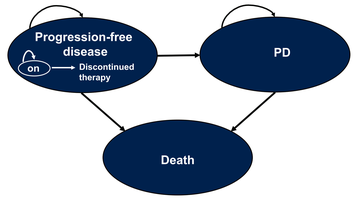
INTRODUCTION

- Ibrutinib, the first-in-class Bruton tyrosine kinase inhibitor (BTKi), and follow-on BTKi, zanubrutinib, are approved for treatment of Waldenström macroglobulinemia (WM)[1,2]
- Ibrutinib is approved as either single-agent therapy or in combination with rituximab[1]
  - Sustained single-agent efficacy and safety were demonstrated in patients with previously untreated WM (NCT02604511)[3]
  - In a phase 3 randomized trial, ibrutinib plus rituximab demonstrated superior progression-free survival (PFS) and longer time to next treatment versus rituximab alone[4]
- Safety and efficacy of ibrutinib versus zanubrutinib for treatment of WM were evaluated in the phase 3 ASPEN study[5]
- Ibrutinib prescribing information includes guidelines for dose reduction (DR) for management of different types and grades of adverse events (AEs)[1]
- Data from clinical trials demonstrated similar efficacy in patients who had ibrutinib DR versus standard-dose ibrutinib, which was subsequently also demonstrated in real-world evidence (RWE) studies[6]
- Here we examined clinical benefits and associated treatment-related and AE-related costs using published clinical trial data and RWE

METHODS

- A semi-Markov model was used to examine clinical and economic outcomes associated with first-line (1L) WM; model features and parameters are described below
- Medical costs (physician visits and monitoring) and AE-related costs were estimated over 1-year/5-year time horizons (THs). AE costs per treated patient per month (PTPPM) were applied over a 1-year TH due to inconsistent reporting across trials at longer time points
- Base case analyses of ibrutinib, zanubrutinib, and bendamustine plus rituximab (BR) were modeled using efficacy and discontinuation data from analyses of United States prescribing information (USPI) and pivotal trials in the 1L WM setting (**Supplementary Table 1**)
  - AE rates were taken from trials reported in USPI and supplemented by values from the literature where specific AE-data were missing from USPIs. Scenario analyses included head-to-head safety and efficacy data for likewise comparisons when available
- Efficacy and safety of ibrutinib and zanubrutinib were evaluated using a scenario analysis based on data from the ibrutinib-zanubrutinib head-to-head trial (ASPEN)[5]
- 1-way sensitivity analyses were conducted assuming a ±20% range in values, and were reported based on the top 5 largest impacts among AE-related costs
- Probabilistic sensitivity analyses were conducted on the incremental PTPPM costs of ibrutinib relative to BR and zanubrutinib
- The impact of ibrutinib DR on costs was examined in scenario analyses using assumptions based on RWE and in a single-center study, including patients eligible for DR following an AE
  - Sarosiek et al[6] found that patients with WM treated with 1L ibrutinib who had a DR following an AE had shorter inpatient hospital stays (mean ± SD, 0.7 ± 0.3 days vs 1.5 ± 1.9 days), had lower number of all-cause 30-day readmission visits, and a lower proportion had post-acute stays (not available vs 14%) compared with patients without a DR
  - Although the number of emergency department and physician office visits were slightly higher in patients with DR, overall WM-related healthcare resource utilization (HCRU) costs were 20.1% lower than in those without DR ($11,944 vs $14,957)

Semi-Markov Model With Weekly Cycles Consistent With Published Model Structure on Similar Decision Problems



- Patients begin in progression-free disease and remain on treatment until progression or discontinuation
- Progression-free disease transition based on treatment-specific PFS curve
- Death based on OS curve and background mortality

OS, overall survival; PD, progressive disease.

Semi-Markov Model Features and Parameters

Perspective	Payer with Medicare population
TH	1 year and 5 years
Cycle length	Weekly
Discount rate	Undiscounted for clinical outcomes due to short TH and key outcomes of study; 3.0% for costs
Mortality	Trial mortality data were used up to a common OS time point across trials of interest; thereafter, the highest mortality data from trial data or background mortality (from National Vital Statistics System) were used, as opposed to using an aggregate of both background mortality or trial data
Discontinuation	Patients who discontinued treatment remained progression free until the transition to PD, based on delta between time to treatment discontinuation and median PFS; in some instances, the risk of discontinuation was limited to the number of patients discontinuing the clinical trial; the number of patients discontinuing was limited to the number observed in the clinical trial
Population	Patients with previously untreated WM
Population, baseline characteristics	Average age (70 years), sex (female, 70%), and body weight (79 kg) were generally consistent with INNOVATE;[4] background mortality from National Vital Statistics System
Comparators	Ibrutinib and zanubrutinib (treated to PD or discontinued due to unacceptable toxicity); BR (6 cycles)
Clinical inputs and sources	Efficacy (PFS, OS), safety (grade 3+ AEs), and discontinuation taken from pivotal trials reported in USPIs for each comparator and corresponding publications, with scenario analyses based on the head-to-head trial of ibrutinib and zanubrutinib (ASPEN)[5]
Economic inputs	Health-state–related HCRU (based on published treatment guidelines and published WM models) and grade 3+ AE costs (based on values from economic evaluations from models), accounting for reduced AE costs associated with ibrutinib DR using assumptions based on RWE
Outcomes	Clinical: PFS, PD, and total life years over model TH Economic: treatment-related costs, AE costs, and total incremental costs (exclusive of treatment acquisition) reported as PTPPM

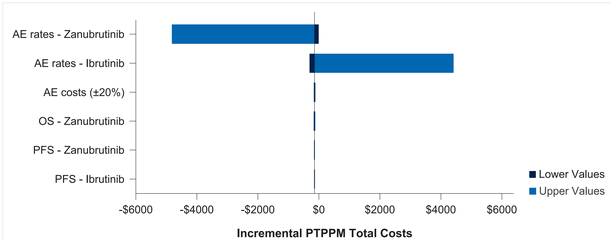
RESULTS

Clinical Results and Estimated Costs

Comparator	Clinical Data Source	Clinical Outcomes (years) PFS (1 year/5 years)	Clinical Outcomes (years) Life Year (1 year/5 years)	Costs (PTPPM) Treatment Related (1 year/5 years)	Costs (PTPPM) AE Costs (1 year)
WM Model					
Ibrutinib	NCT02604511	0.97/4.16	0.998/4.85	$60/$62	$677/$540 (DR)[a]
BR	StiL[7]	0.94/3.77	0.98/4.54	$61/$64	$1064
Zanubrutinib	ASPEN[5]	0.92/3.40	0.95/3.81	$59/$61	$820
ASPEN Scenario					
Ibrutinib	ASPEN[5]	0.98/4.49	0.99/4.75	$59/$58	$564
Zanubrutinib	ASPEN[5]	0.92/3.40	0.95/3.81	$59/$61	$578

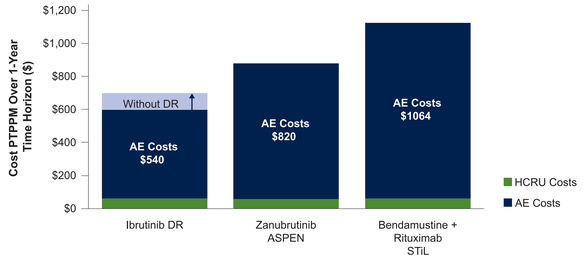
[a]Scenario results assume a 20.1% reduction in ibrutinib AE costs associated with DR as needed based on RWE.

Incremental Total Costs for Ibrutinib Versus Zanubrutinib Are Most Sensitive to AE Rates in 1-Way Sensitivity Analyses



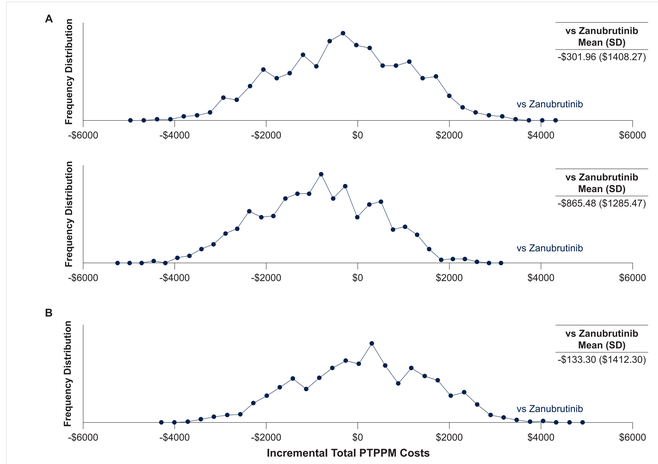
Comparisons calculated over a 1-year TH; 1-way sensitivity analysis evaluated incremental PTPPM total costs based on AE-related costs and routine medical care costs.

Ibrutinib DR Lowered Ibrutinib AE Costs by 20.1%, Resulting in Lower Total Costs for DR-Eligible Ibrutinib Patients Relative to Zanubrutinib and BR



Based on modeled AE costs over a 1-year TH. Model applied assumptions for DR of ibrutinib based on RWE.

Cost Reductions Associated With Ibrutinib DR May Shift Incremental Total Costs Toward More Cost Savings With Ibrutinib Relative to Zanubrutinib in Probabilistic Sensitivity Analyses Using (A) Base Case Data and (B) Head-to-Head Clinical Trial Data



LIMITATIONS

- The implementation of conditional risk of progression relative to survival can produce counterintuitive comparative results in cases where PFS and OS curves are similar, although no standard alternative is considered totally acceptable without the use of individual patient data
- OS for ibrutinib implemented a Jefferies correction due to trial reporting 100% survival
- Base case results were limited to AEs and clinical outcomes as reported in USPI and available clinical trials where gaps remained
- Due to the lack of consistent and quality data for long-term AEs, the cost of AEs only applies to the first modeled year. Aggregated AEs or AE development over time due to prolonged use of either comparator were not captured due to nonstandardized reporting of AEs over time across comparator toxicity sources of interest
- Clinical efficacy and safety comparisons were limited by small trial, subgroup sizes, and differences in treatment durations and exposure
- The impact of DR was modeled as a reduction in AE costs only due to a lack of data regarding not only the relationship between treatment persistence and efficacy but also the relationship between AEs and real-world discontinuation

References

1. IMBRUVICA (ibrutinib) [prescribing information]. South San Francisco, CA: Pharmacyclics LLC; 2024.
2. BRUKINSA (zanubrutinib) [prescribing information]. San Mateo, CA: BeiGene Ltd., 2024.
3. Castillo JJ et al. *Leukemia*. 2022; 36(2):532–539.
4. Buske C et al. *J Clin Oncol*. 2022; 40(1):52–62.
5. Tam CS et al. *Blood*. 2020; 136(18):2038–2050.
6. Sarosiek SR et al. *Blood*. 2023; 142(Suppl1):3780.
7. Rummel MJ et al. *Lancet*. 2013; 381(9873):1203–1210.