

Clinical Outcomes and Associated Costs of Treating Patients With Chronic Lymphocytic Leukemia With Bruton Tyrosine Kinase Inhibitors in the First-Line and Relapsed/Refractory Settings

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SUPPLEMENTAL RESULTS

Supplementary Table 1. Key Clinical and Economic Model Inputs

PARAMETER	INPUT	SOURCE	INPUT	SOURCE	INPUT	SOURCE
	lbrutinib		Acalabrutinib		Zanubrutinib	
EFFICACY INPUTS	PFS, OS		(PFS, OS)		(PFS, OS)	
1L CLL, BASE CASE	86.9%/98.0%	RESONATE-2 (Burger, 2015)	87.0%/95.0%	ELEVATE-TN (Sharman, 2020)	85.5%/94.3%	Sequoia (Tam, 2022)
RR CLL, BASE CASE	70.3%/83.5%	RESONATE (Byrd, 2019)	64.8%/85.8%	ELEVATE DD (Dyrd 2021)	78.4%/89.1%	ALPINE (Brown, 2023)
R/R CLL, ELEVATE-RR SCENARIO	65.0%/85.3%	ELEVATE-RR (Byrd, 2021) ALPINE (Brown, 2023)	64.8%/85.8%	ELEVATE-RR (Byrd, 2021)	78 1%/80 1%	Brown 2023
R/R CLL, MAIC SCENARIO	81.0%/ NR	ALPINE-LIKE RESONATE-2	76.0%/ NR	ALPINE-LIKE ASCENT	78.4%/89.1%	ALPINE (Brown, 2023)
,		(Ghia 2023)		(Kittai, 2023)		, , , ,
SAFETY INPUTS	AE Rate		AE Rate		AE Rate	
1L CLL, BASE CASE	4.00/	Ibrutinih DI	2.20/	ELEVATE TN (Sharman 2020)	6.69/	Zapubrutinih DI
ANEMIA	4.0% 5.9%	RESONATE-2 (Burger 2015)	Z.Z%	Acalabrutinib Pl	0.0%	Zanubrutinib Pl
NEUTROPENIA	10.0%	RESONATE-2 (Burger, 2015)	13.0%	Acalabrutinib PI	12.5%	Seguoia (Tam, 2022)
HEADACHE	1.0%	Ibrutinib PI	1.1%	Acalabrutinib PI	0.6%	Zanubrutinib PI
DIARRHEA	4.0%	Ibrutinib PI	0.6%	Acalabrutinib PI	0.9%	Zanubrutinib PI
PNEUMONIA	8.0%	Ibrutinib PI	4.5%	Acalabrutinib PI	6.0%	Zanubrutinib PI
THROMBOCYTOPENIA	2.2%	RESONATE-2 (Burger, 2015)	3.4%	Acalabrutinib PI	1.4%	Sequoia (Tam, 2022)
ATRIAL FIBRILLATION	1.5%	RESONATE-2 (Burger, 2015)	0.0%	ELEVATE-TN (Sharman, 2020)	2.0%	Sequoia (Tam, 2022)
INFECTION	9.6%	RESONATE-2 (Burger, 2015)	9.5%	ELEVATE-TN (Sharman, 2020)	9.7%	Sequoia (Tam, 2022)
FAIIGUE	1.0%	Ibrutinib PI	1.1%	Acalabrutinib Pl	1.1%	Zanubrutinib Pl
HEMORRHAGE	4.0%	RESONATE-2 (Burger 2015)	1.7%	Acalabrutinib Pl	4.3%	Zanubrutinib Pl
ARTHRALGIA	1.0%	Ibrutinib PI	0.6%	Acalabrutinib PI	0.9%	Sequoia (Tam, 2022)
NAUSEA	1.0%	Ibrutinib PI	0.0%	Acalabrutinib PI	0.0%	Zanubrutinib PI
SEPSIS	0.0%	NR	0.0%	ELEVATE-TN (Sharman, 2020)	0.9%	Sequoia (Tam, 2022)
R/R CLL, BASE CASE	lbrutinib		Acalabrutinib		Zanubrutinib	
HYPERTENSION	8.0%	Byrd 2019	2.0%	ASCEND (Ghia 2020)	13%	Zanubrutinib PI
	5.0%	RESONATE (Byrd, 2014)	15.0%	Acalabrutinib Pl	2.2%	ALPINE (Brown, 2023)
HEADACHE	16.0%	RESONATE (Byra, 2014)	23.0%	Acalabrutinib Pl	16.0%	ALPINE (Brown, 2023)
DIARRHEA	4.0%	Ibrutinib PI	1.3%	Acalabrutinib PI	1.5%	Zanubrutinib PI
PNEUMONIA	12.0%	Ibrutinib PI	5.0%	ASCEND (Ghia 2020)	9.0%	Zanubrutinib PI
THROMBOCYTOPENIA	6.0%	RESONATE (Byrd, 2014)	6.0%	Acalabrutinib PI	2.8%	ALPINE (Brown, 2023)
ATRIAL FIBRILLATION	3.0%	RESONATE (Byrd, 2014)	1.9%	ASCEND (Ghia 2020)	1.9%	ALPINE (Brown, 2023)
INFECTION	16.0%	RESONATE (Byrd, 2014)	8.5%	Acalabrutinib PI	8.3%	ALPINE (Hillmen, 2022)
FATIGUE	2.0%	RESONATE (Byrd, 2014)	1.9%	Acalabrutinib PI	0.9%	ALPINE (Brown, 2023)
TUMOR LYSIS SYNDROME	0.0%	ALIPINE (Hillman 2020)	0%		0 %	ALPINE (Brown, 2023)
KASH HEMODDUACE	J.U%		U%	ASCEND (Ghia 2020)	1.2%	∠anubrutinib Pl
	1.0%	Ibrutinib Pl	1.3%	Acalabrutinib Pl	2.5%	Zanubrutinib Pl
NAUSEA	2.0%	Ibrutinib PI	0%	ASCEND (Ghia 2020)	0%	NR
SEPSIS	1.0%	RESONATE (Byrd, 2014)	1.50%	Assumption based on ELEVATE-	0.5%	ALPINE (Hillmen, 2022)
				RR		
R/R CLL, ELEVATE-RR SCENARIO	Ibrutinib		Acalabrutinib			
HYPERTENSION	8.7%	ELEVATE-RR (Byrd, 2021)	4.1%	ELEVATE-RR (Byrd, 2021)		
	12.9%	ELEVATE-RR (Byrd, 2021)	10.5%	ELEVATE-RR (Byrd, 2021) ELEVATE-RR (Byrd, 2021)		
HEADACHE	0%	ELEVATE-RR (Byrd, 2021)	1.5%	ELEVATE-RR (Byrd, 2021)		
DIARRHEA	4.9%	ELEVATE-RR (Byrd, 2021)	1.1%	ELEVATE-RR (Byrd, 2021)		
PNEUMONIA	8.7%	ELEVATE-RR (Byrd, 2021)	10.5%	ELEVATE-RR (Byrd, 2021)		
THROMBOCYTOPENIA	6.8%	ELEVATE-RR (Byrd, 2021)	9.8%	ELEVATE-RR (Byrd, 2021)		
ATRIAL FIBRILLATION	3.4%	ELEVATE-RR (Byrd, 2021)	4.5%	ELEVATE-RR (Byrd, 2021)		
INFECTION	21.3%	ELEVATE-RR (Byrd, 2021)	20.3%	ELEVATE-RR (Byrd, 2021)		
FATIGUE	0%	ELEVATE-RR (Byrd, 2021)	3.4%	ELEVATE-RR (Byrd, 2021)		
RASH	0%	ELEVATE-RR (Byrd, 2021) ELEVATE-RR (Byrd, 2021)	2%	ELEVATE-RR (Byrd, 2021)		
HEMORRHAGE	0%	ELEVATE-IRR (Byrd, 2021)	0%	ELEVATE-RR (Byrd, 2021)		
ARTHRALGIA	0.8%	ELEVATE-RR (Byrd, 2021)	0%	ELEVATE-RR (Byrd, 2021)		
NAUSEA	0.4%	ELEVATE-RR (Byrd, 2021)	0%	ELEVATE-RR (Byrd, 2021)		
SEPSIS	0%	ELEVATE-RR (Byrd, 2021)	0%	ELEVATE-RR (Byrd, 2021)		
CLL R/R, ALPINE SCENARIO	lbrutinib				Zanubrutinib	
HYPERTENSION	11.1%	ALPINE (Brown, 2023)			14.8%	ALPINE (Brown, 2023)
	2.5%	ALPINE (Brown, 2023)			2.2%	ALPINE (Brown, 2023)
	13.9%	ALPINE (Brown, 2023)			16%	ALPINE (Brown, 2023)
	0%	ALPINE (BIOWI, 2023)			0%	ALPINE (Brown, 2023)
PNEUMONIA	12%	ALPINE (Brown, 2023)			13%	ALPINE (Brown, 2023)
THROMBOCYTOPENIA	3.7%	ALPINE (Brown, 2023)			2.8%	ALPINE (Brown, 2023)
ATRIAL FIBRILLATION	3.7%	ALPINE (Brown, 2023)			1.9%	ALPINE (Brown, 2023)
INFECTION	16.1%	ALPINE (Brown, 2023)			13.5%	ALPINE (Brown, 2023)
FATIGUE	0%	ALPINE (Brown, 2023)			0%	ALPINE (Brown, 2023)
	U%	ALPINE (Brown, 2023)			U%	ALPINE (Brown, 2023)
HEMORRHAGE	0%	ALFINE (DIUWII, 2023)			0%	ALFINE (BIOWN, 2023)
ARTHRALGIA	0%	ALPINE (Brown, 2023)			0%	ALPINE (Brown. 2023)
NAUSEA	0%	ALPINE (Brown, 2023)			0%	ALPINE (Brown, 2023)
SEPSIS	0%	ALPINE (Brown, 2023)			0%	ALPINE (Brown, 2023)
COST INPUTS ^a	Cost					
1L CLL/SLL ANNUAL HCRU-COSTS						
PROGRESSION FREE DISEASE	\$510	Munir 2023				
RIR CITISIT ANNUAL HODIL COSTS	φ ∠, ∀∀4					
PROGRESSION FREE DISFASE	\$1,000	Barbier 2022: Munir 2023				
PROGRESSED DISEASE	\$2,520	Barbier 2022; Munir 2023			<u></u>	
ADVERSE EVENT COSTS						
HYPERTENSION	\$5,417	Munir, 2023				
ANEMIA	\$8,800	Munir, 2023				
NEUTROPENIA	\$14,529	Munir, 2023				
	ቅሀ	Assumption Munit 2023				
	φ0,070 \$9.427	Chatteriee 2021				
THROMBOCYTOPENIA	\$14,529	Munir, 2023				
ATRIAL FIBRILLATION	\$11,894	Munir, 2023				
INFECTION	\$10,801	Munir, 2023				
FATIGUE	\$744	Munir, 2023				
TUMOR LYSIS SYNDROME	\$23,311	Munir, 2023				
RASH	\$5,891	Munir, 2023				
	\$27,071	Macrosov 2022				
	30,071 \$7 062	McGregor 2023				
SEPSIS	\$20.851	Chatteriee, 2021				

^aAll costs are inflated to May 2023. 1L, first-line, CLL, chronic lymphocytic leukemia, HCRU, healthcare resource utilization; NR, not reached; OS, overall survival; PFS, progression free survival; PI, prescribing information; R/R, relapsed/refractory; SLL, small lymphocytic leukemia.

Supplementary Figure 1. Cost Reductions Associated With Ibrutinib DR May Shift Incremental Total Costs Toward Cost Savings With Ibrutinib Relative to Acalabrutinib or Zanubrutinib Among Patients Who May Be Eligible for DR Following an AE





1L, first line; AE, adverse event; CLL, chronic lymphocytic leukemia; PTPPM, per treated patient per month; R/R, relapsed/refractory; SD, standard deviation.

Supplementary Figure 2. Costs Calculated Using Head-to-Head Efficacy and Safety Are Slightly Higher for Ibrutinib Versus Acalabrutinib and Very Similar for Ibrutinib Versus Zanubrutinib





CLL, chronic lymphocytic leukemia; PTPPM, per treated patient per month; R/R, relapsed/refractory; SD, standard deviation.