

Title: Real-World Outcomes among Medicare Beneficiaries Treated with Bruton Tyrosine Kinase Inhibitors for Treatment-Naive CLL

Authors: Daniel Ermann¹, Deborah M. Stephens², Xiaoliang Wang³, Irene Varghese⁴, Heidi De Souza⁴, Caitlin Sheetz⁴, Qianhong Fu³, Gregory A. Maglinte³, Rhys Williams³, Erlene K. Seymour³, Derrick van Beuge³, Mazyar Shadman⁵, and Ryan Jacobs⁶

Affiliations: ¹Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; ²University of North Carolina School of Medicine, Chapel Hill, NC, USA; ³BeOne Medicines, Ltd, San Carlos, CA, USA; ⁴ADVI Health, Washington DC, USA; ⁵Fred Hutchinson Cancer Center, University of Washington, Seattle, WA, USA; ⁶Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA

Corresponding Author: Daniel Ermann, Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA. Email: daniel.ermann@hci.utah.edu

Supplementary Figures

Figure 1. Real-World Time to Discontinuation by Age Cohort. a) Age Cohort Between 65 and 74 Years of Age; b) Age Cohort of 75 to 84 Years of Age; and c) 85 Years of Age and Older

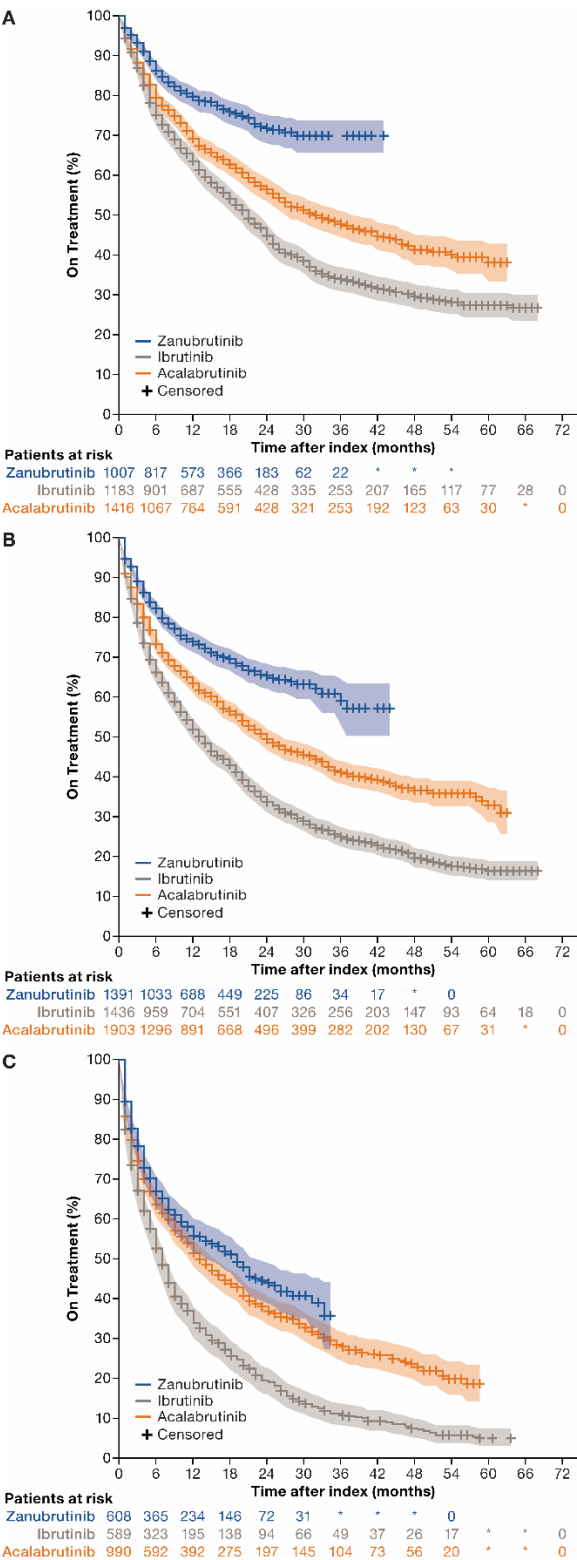


Figure 2. Real-World Time to Next Treatment by Age Cohort. a) Age Cohort Between 65 and 74 Years of Age; b) Age Cohort of 75 to 84 Years of Age; and c) 85 Years of Age and Older

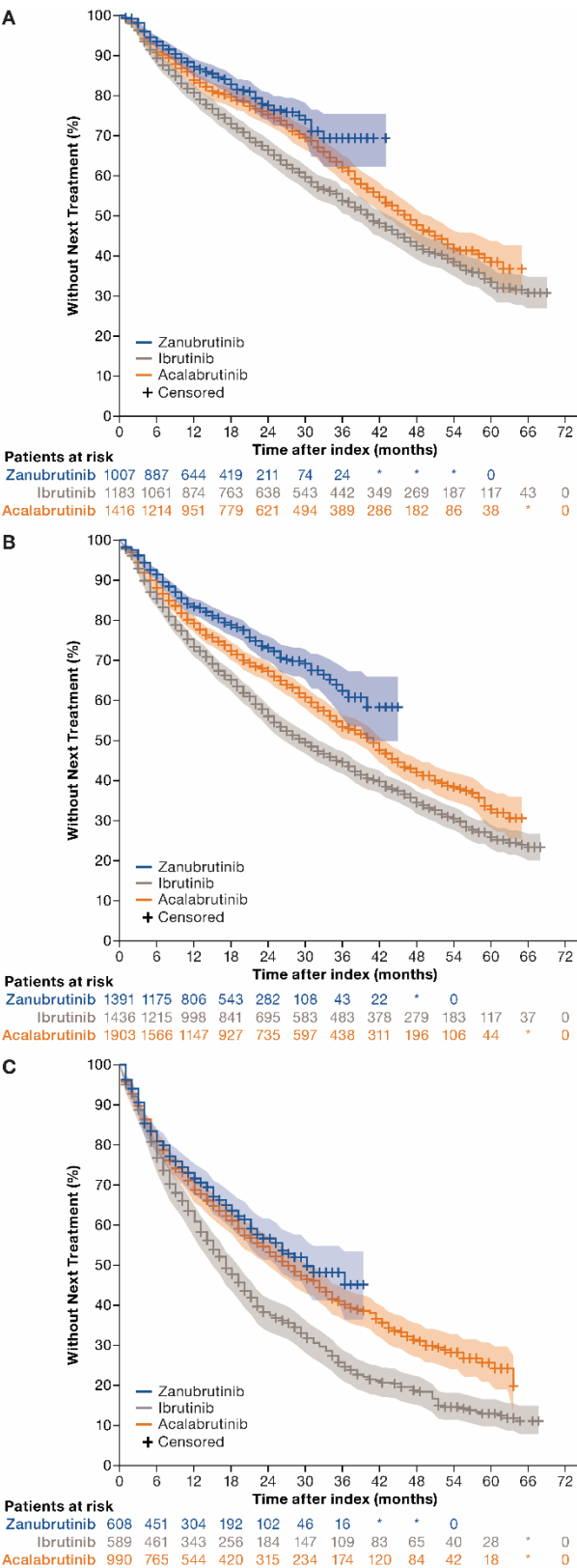
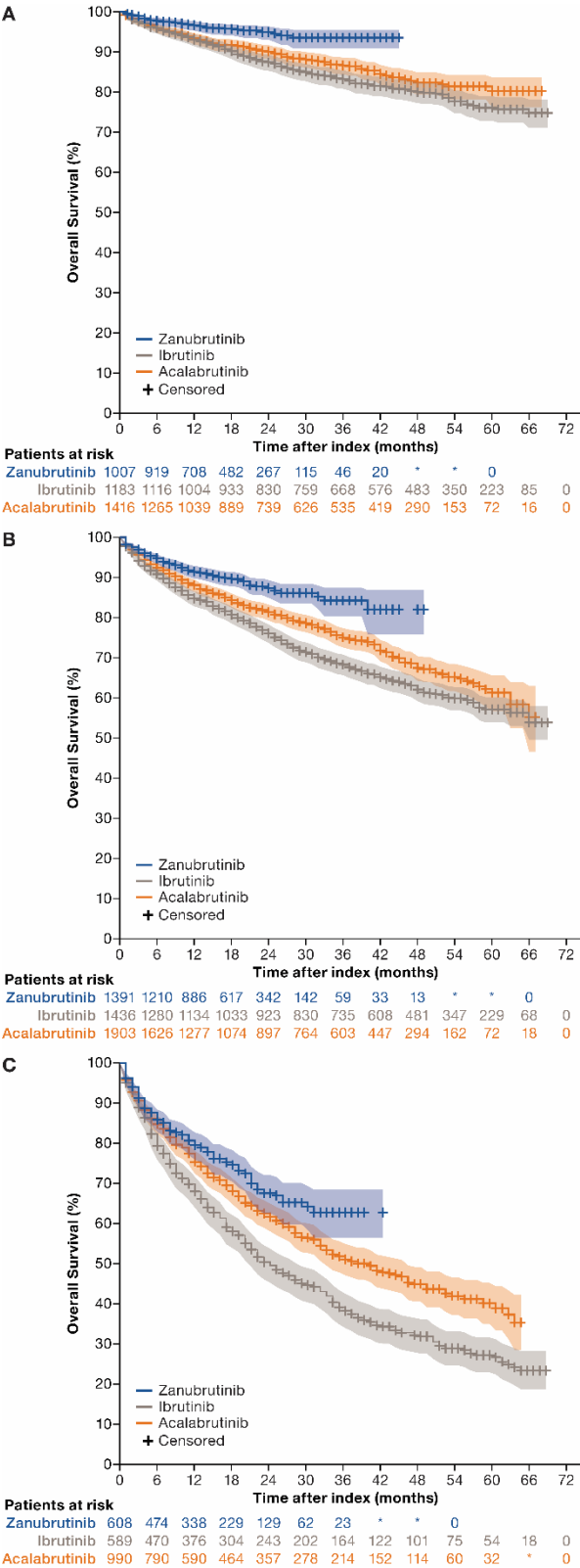


Figure 3. Real-World Overall Survival by Age Cohort. a) Age Cohort Between 65 and 74 Years of Age; b) Age Cohort of 75 to 84 Years of Age; and c) 85 Years of Age and Older



Supplementary Tables

Supplementary Table 1. rwTTD Analysis of Ibrutinib or Acalabrutinib as Reference Versus Zanubrutinib by Age Group Using Cox Proportional Hazards Regression

Age Group	Outcome	Zanubrutinib	Ibrutinib [†]	Acalabrutinib [†]
65-74	12-month rwTTD, % (95% CI)	79.7 (77.0, 82.2)	63.5 (60.7, 66.3)	69.2 (66.6, 71.7)
	24-month rwTTD, % (95% CI)	71.8 (68.1, 75.2)	44.8 (41.7, 47.8)	56.5 (53.4, 59.4)
	Unadjusted HR (95% CI)	—	0.44 (0.38, 0.51)	0.58 (0.50, 0.68)
	P value (unadjusted)	—	<.001	<.001
	Adjusted HR (95% CI) [‡]	—	0.59 (0.48, 0.72)	0.75 (0.62, 0.89)
	P value (adjusted)	—	<.001	.001
75-84	12-month rwTTD, % (95% CI)	73.9 (71.3, 76.2)	51.9 (49.2, 54.5)	63.4 (61.1, 65.7)
	24-month rwTTD, % (95% CI)	65.3 (62.1, 68.4)	33.7 (31.1, 36.3)	49.4 (46.7, 52.0)
	Unadjusted HR (95% CI)	—	0.43 (0.39, 0.49)	0.64 (0.56, 0.72)
	P value (unadjusted)	—	<.001	<.001
	Adjusted HR (95% CI) [‡]	—	0.54 (0.46, 0.64)	0.83 (0.73, 0.96)
	P value (adjusted)	—	<.001	.009
≥85	12-month rwTTD, % (95% CI)	55.8 (51.4, 60.0)	33.9 (30.0, 37.9)	51.4 (48.1, 54.7)
	24-month rwTTD, % (95% CI)	43.9 (38.7, 48.9)	19.1 (15.9, 22.6)	36.8 (33.3, 40.4)
	Unadjusted HR (95% CI)	—	0.54 (0.47, 0.62)	0.85 (0.73, 0.98)
	P value (unadjusted)	—	<.001	.02
	Adjusted HR (95% CI) [‡]	—	0.60 (0.49, 0.75)	1.0 (0.86, 1.2)
	P value (adjusted)	—	<.001	.92

aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; ref, reference; rwTTD, real-world time to treatment discontinuation.

[†]Denotes reference group versus zanubrutinib.

[‡]Adjusted covariates included categorical age (65-74, 75-84, and ≥85), sex, race/ethnicity (non-Hispanic White versus other), CCI score (0, 1-2, 3-4, ≥5), and year of index.

Supplementary Table 2. rwTTNT Analysis of Ibrutinib or Acalabrutinib as Reference Versus Zanubrutinib by Age Group Using Cox Proportional Hazards Regression

Age Group	Outcome	Zanubrutinib	Ibrutinib [†]	Acalabrutinib [†]
65-74	12-month rwTTNT, % (95% CI)	87.2 (84.8, 89.2)	80.7 (78.3, 82.9)	83.9 (81.8, 85.9)
	24-month rwTTNT, % (95% CI)	77.6 (73.9, 80.9)	66.4 (63.5, 69.2)	75.4 (72.7, 77.8)
	Unadjusted HR (95% CI)	—	0.60 (0.50, 0.71)	0.80 (0.67, 0.97)
	<i>P</i> value (unadjusted)	—	<.001	.02
	Adjusted HR (95% CI) [‡]	—	0.62 (0.49, 0.78)	0.82 (0.67, 1.0)
	<i>P</i> value (adjusted)	—	<.001	.06
75-84	12-month rwTTNT, % (95% CI)	83.4 (81.1, 85.4)	73.4 (71.0, 75.6)	79.2 (77.2, 81.1)
	24-month rwTTNT, % (95% CI)	73.1 (69.9, 76.0)	56.1 (53.3, 58.7)	67.3 (64.8, 69.6)
	Unadjusted HR (95% CI)	—	0.56 (0.49, 0.64)	0.75 (0.65, 0.87)
	<i>P</i> value (unadjusted)	—	<.001	<.001
	Adjusted HR (95% CI) [‡]	—	0.58 (0.49, 0.71)	0.83 (0.71, 0.97)
	<i>P</i> value (adjusted)	—	<.001	.02
≥85	12-month rwTTNT, % (95% CI)	71.6 (67.6, 75.2)	60.9 (56.7, 64.8)	68.7 (65.6, 71.7)
	24-month rwTTNT, % (95% CI)	56.7 (51.4, 61.6)	37.4 (33.3, 41.5)	53.2 (49.6, 56.7)
	Unadjusted HR (95% CI)	—	0.64 (0.54, 0.76)	0.92 (0.78, 1.1)
	<i>P</i> value (unadjusted)	—	<.001	.30
	Adjusted HR (95% CI) [‡]	—	0.71 (0.55, 0.91)	0.99 (0.82, 1.2)
	<i>P</i> value (adjusted)	—	.003	.90

aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; ref, reference; rwTTNT, real-world time to next treatment.

[†]Denotes reference group versus zanubrutinib.

[‡]Adjusted covariates included categorical age (65-74, 75-84, and ≥ 85), sex, race/ethnicity (non-Hispanic White versus other), CCI score (0, 1-2, 3-4, ≥5), and year of index.

Supplementary Table 3. rwOS Analysis of Ibrutinib or Acalabrutinib as Reference Versus Zanubrutinib by Age Group Using Cox Proportional Hazards Regression

Age Group	Outcome	Zanubrutinib	Ibrutinib [†]	Acalabrutinib [†]
65–74	12-month rwOS, % (95% CI)	96.7 (95.3, 97.7)	93.0 (91.4, 94.4)	93.4 (91.9, 94.6)
	24-month rwOS, % (95% CI)	94.9 (93.0, 96.3)	87.4 (85.3, 89.2)	90.1 (88.2, 91.7)
	Unadjusted HR (95% CI)	–	0.42 (0.30, 0.59)	0.55 (0.36, 0.71)
	P value (unadjusted)	–	< .001	< .001
	Adjusted HR (95% CI) [‡]	–	0.56 (0.36, 0.86)	0.55 (0.38, 0.81)
	P value (adjusted)	–	.008	.002
75–84	12-month rwOS, % (95% CI)	91.4 (89.7, 92.9)	84.8 (82.8, 86.6)	88.1 (86.5, 89.5)
	24-month rwOS, % (95% CI)	87.3 (84.9, 89.3)	76.1 (73.7, 78.3)	81.4 (79.3, 83.2)
	Unadjusted HR (95% CI)	–	0.50 (0.41, 0.61)	0.65 (0.53, 0.79)
	P value (unadjusted)	–	< .001	< .001
	Adjusted HR (95% CI) [‡]	–	0.66 (0.50, 87)	0.73 (0.59, 0.91)
	P value (adjusted)	–	.003	.005
≥85	12-month rwOS, % (95% CI)	79.5 (75.8, 82.7)	68.0 (64.0, 71.6)	75.4 (72.4, 78.1)
	24-month rwOS, % (95% CI)	67.5 (62.5, 72.1)	49.6 (45.3, 53.7)	61.6 (58.0, 65.0)
	Unadjusted HR (95% CI)	–	0.67 (0.48, 0.70)	0.81 (0.67, 0.98)
	P value (unadjusted)	–	< .001	.03
	Adjusted HR (95% CI) [‡]	–	0.67 (0.51, 0.88)	0.91 (0.73, 1.1)
	P value (adjusted)	–	.004	.35

aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; ref, reference; rwOS, real-world overall survival.

[†]Denotes reference group versus zanubrutinib.

[‡]Adjusted covariates included categorical age (65-74, 75-84, and ≥ 85), sex, race/ethnicity (non-Hispanic White versus other), CCI score (0, 1-2, 3-4, ≥ 5), and year of index.