

Cumulative review of hypertension in patients with chronic lymphocytic leukemia treated with acalabrutinib

Authors

Alessandra Ferrajoli,¹ George Follows,² Yotvat Marmor,³ Jack Roos,⁴ Naghmana Bajwa,⁴ Venkata Madhira,⁵ Kenji Nozaki,⁶ Paulo Miranda,⁴ Dinci Pennap⁴ and Krish Patel⁷

¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Addenbrookes Hospital, Cambridge, UK; ³AstraZeneca, South San Francisco, CA, USA; ⁴AstraZeneca, Gaithersburg, MD, USA; ⁵AstraZeneca, Wilmington, DE, USA; ⁶AstraZeneca, Osaka, Japan and ⁷Swedish Cancer Institute, Seattle, WA, USA

Correspondence:

A. FERRAJOLI - aferrajo@mdanderson.org

<https://doi.org/10.3324/haematol.2024.285757>

Received: April 26, 2024.

Accepted: October 31, 2024.

Early view: November 7, 2024.

©2025 Ferrata Storti Foundation

Published under a CC BY-NC license 

Supplemental Information

Supplemental Table 1. Study summaries

Study Name	Study Description	Treatments	Number of Patients
15-H-0016 (NCT02337829)	Phase II study in patients with R/R CLL/SLL or TN CLL/SLL with del(17p)	Acalabrutinib monotherapy	48 (TN, n=16; R/R, n=32)
ACE-CL-001 (NCT02029443)	Phase I–II study in patients with TN or R/R CLL/SLL	Acalabrutinib monotherapy	301 (TN, n=99; R/R, n=202)
ACE-CL-003 (NCT02296918)	Phase Ib study in patients with TN or R/R CLL/SLL	Acalabrutinib + obinutuzumab	45 (TN, n=19; R/R, n=26)
ACE-CL-006 (NCT02477696; ELEVATE-RR)	Phase III study in patients with R/R CLL	Acalabrutinib monotherapy vs ibrutinib	529 (R/R, n=529)
ACE-CL-007 (NCT02475681; ELEVATE-TN)	Phase III study in patients with TN CLL	Acalabrutinib monotherapy or acalabrutinib + obinutuzumab vs obinutuzumab + chlorambucil	526 (TN, n=526)
ACE-CL-309 (NCT02970318; ASCEND)	Phase III study in patients with R/R CLL	Acalabrutinib monotherapy vs idelalisib + rituximab or bendamustine + rituximab	307 (R/R, n=307)

CLL, chronic lymphocytic leukemia; R/R, relapsed/refractory; SLL, small lymphocytic lymphoma; TN, treatment naive.

Supplemental Table 2. Patient demographics and baseline characteristics

Characteristic	Acalabrutinib Monotherapy (N=947)	Acalabrutinib + Obinutuzumab (N=223)	Ibrutinib ^a (N=264)	Comparators ^b (N=322)
Age, median (range), y	67 (32–89)	69 (41–88)	65 (28–88)	69 (34–91)
<i>P</i> -value*	–	0.0024	0.5552	<0.0001
Male, n (%)	636 (67.2)	143 (64.1)	193 (73.1)	202 (62.7)
<i>P</i> -value*	–	0.3875	0.0660	0.1474
PMH of hypertension, n (%) ^c	513 (54.2)	147 (65.9)	128 (48.5)	193 (59.9)
<i>P</i> -value*	–	0.0015	0.1017	0.0720
Number of concomitant antihypertensive agents, n (%)				
1	154 (16.3)	43 (19.3)	53 (20.1)	51 (15.8)
<i>P</i> -value*	–	0.2781	0.1455	0.8585
2	106 (11.2)	40 (17.9)	37 (14.0)	42 (13.0)
<i>P</i> -value*	–	0.0061	0.2090	0.3716
3	54 (5.7)	19 (8.5)	13 (4.9)	24 (7.5)
<i>P</i> -value*	–	0.1175	0.6249	0.2584
>3	29 (3.1)	10 (4.5)	18 (6.8)	13 (4.0)
<i>P</i> -value*	–	0.2872	0.0052	0.3982
Body mass index, kg/m ²				
Mean (SD)	27.3 (5.0)	27.9 (5.4)	27.3 (4.9)	27.2 (4.9)
Median (range)	26.6 (15.8–48.9)	27.0 (18.1–50.5)	27.1 (17.8–54.5)	26.7 (15.6–46.3)
<i>P</i> -value*	–	0.3061	0.9984	0.9880

Body mass index category (kg/m ²), n (%)				
25 to <30 (overweight)	391 (41.3)	86 (38.6)	113 (42.8)	131 (40.7)
<i>P</i> -value*	–	0.4566	0.6588	0.8488
≥30 (obese)	223 (23.5)	62 (27.8)	64 (24.2)	81 (25.2)
<i>P</i> -value*	–	0.1830	0.8145	0.5594
Smoking status (yes), n/N (%) ^d	184/443 (41.5)	76/178 (42.7)	110/264 (41.7)	76/169 (45.0)
Former, n (%)	153 (34.5)	56 (31.5)	84 (31.8)	56 (33.1)
<i>P</i> -value*	–	0.0007	<.0001	0.6376
Current, n (%)	31 (7.0)	20 (11.2)	26 (9.8)	20 (11.8)
<i>P</i> -value*	–	0.0002	<0.0001	0.0204
Chronic kidney disease, n (%) ^e	67 (7.1)	12 (5.4)	19 (7.2)	18 (5.6)
<i>P</i> -value*	–	0.3645	0.9456	0.3572
Sleep apnea syndrome, n (%)	52 (5.5)	15 (6.7)	8 (3.0)	14 (4.3)
<i>P</i> -value*	–	0.4750	0.1033	0.4248
Diabetes mellitus ^f	177 (18.7)	58 (26.0)	50 (18.9)	64 (19.9)
<i>P</i> -value*	–	0.0141	0.9270	0.6395
Dyslipidemia ^g	264 (27.9)	86 (38.6)	64 (24.2)	94 (29.2)
<i>P</i> -value*	–	0.0017	0.2399	0.6506

CLL, chronic lymphocytic leukemia; MedDRA, Medical Dictionary for Regulatory Activities; PMH, past medical history; R/R, relapsed/refractory; SD, standard deviation; SMQ, Standardized MedDRA Query; y, years.

*Versus acalabrutinib monotherapy.

^aPatients with R/R CLL from ELEVATE-RR.

^bPatients with CLL treated with obinutuzumab + chlorambucil (ELEVATE-TN), idelalisib + rituximab (ASCEND), or bendamustine + rituximab (ASCEND).

^cPMH of hypertension defined as MedDRA v25.1 (narrow) hypertension SMQ.

^dAmong patients whose smoking habits were collected.

^eAggregate term that includes the following terms: chronic kidney disease, dialysis, dialysis device insertion, glomerulonephritis chronic, hyperparathyroidism secondary, kidney fibrosis, and renal failure.

^fAggregate term that includes the following terms: blood glucose increased, diabetes mellitus, gestational diabetes, glucose tolerance impaired, glycosylated hemoglobin increased, hyperglycemia, impaired fasting glucose, insulin resistance, steroid diabetes, type 1 diabetes mellitus, type 2 diabetes mellitus, and type 3 diabetes mellitus.

^gAggregate term that includes the following terms: blood cholesterol increased, blood triglycerides increased, diabetic dyslipidemia, dyslipidemia, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia, lipid metabolism disorder, lipids abnormal, lipoprotein (a) increased, metabolic syndrome, type IIa hyperlipidemia, type V hyperlipidemia.

Supplemental Table 3. Patient demographics and baseline characteristics in patients who experienced hypertension

Characteristic	Acalabrutinib Monotherapy (N=147)	Acalabrutinib + Obinutuzumab (N=39)	Ibrutinib ^a (N=71)	Comparators ^b (N=13)
Age, median (range), y	65 (44–85)	67 (44–88)	65 (49–83)	66 (43–84)
<i>P</i> -value*	–	0.5883	0.7832	0.7061
Male, n (%)	97 (66.0)	26 (66.7)	53 (74.6)	12 (92.3)
<i>P</i> -value*	–	0.9364	0.1958	0.0509
PMH of hypertension, n (%) ^c	88 (59.9)	30 (76.9)	33 (46.5)	7 (53.8)
<i>P</i> -value*	–	0.0492	0.0624	0.6720
Number of concomitant antihypertensive agents, n (%)				
1	29 (19.7)	10 (25.6)	26 (36.6)	5 (38.5)
<i>P</i> -value*	–	0.4200	0.0071	0.1135
2	18 (12.2)	9 (23.1)	14 (19.7)	3 (23.1)
<i>P</i> -value*	–	0.0878	0.1440	0.2676
3	10 (6.8)	5 (12.8)	4 (5.6)	2 (15.4)
<i>P</i> -value*	–	0.2198	0.7415	0.2602
>3	9 (6.1)	1 (2.6)	8 (11.3)	1 (7.7)
<i>P</i> -value*	–	0.3811	0.1843	0.8227
Body mass index, kg/m ²				
Mean (SD)	27.5 (4.8)	27.5 (4.1)	28.2 (5.7)	27.1 (4.8)

Median (range)	26.7 (15.8–45.0)	27.3 (18.7–36.4)	27.4 (19.3–54.5)	26.3 (19.6–35.0)
<i>P</i> -value*	–	1.0000	0.7197	0.9943
Body mass index category (kg/m ²), n (%)				
25 to <30 (overweight)	58 (39.5)	18 (46.2)	33 (46.5)	3 (23.1)
<i>P</i> -value*	–	0.4494	0.3244	0.2438
≥30 (obese)	40 (27.2)	9 (23.1)	19 (26.8)	4 (30.8)
<i>P</i> -value*	–	0.6024	0.9441	0.7830
Smoking status (yes), n (%) ^d	16/44 (36.4)	6/17 (35.3)	34/71 (47.9)	3/6 (50.0)
Former	15 (34.1)	6 (35.3)	28 (39.4)	2 (33.3)
<i>P</i> -value*	–	0.3635	<0.0001	0.5612
Current	1 (2.3)	0	6 (8.5)	1 (16.7)
<i>P</i> -value*	–	N/C	N/C	N/C
Chronic kidney disease, n (%) ^e	12 (8.2)	2 (5.1)	5 (7.0)	2 (15.4)
<i>P</i> -value*	–	0.5230	0.7724	0.3771
Sleep apnea syndrome, n (%)	9 (6.1)	7 (17.9)	4 (5.6)	0
<i>P</i> -value*	–	N/C	N/C	N/C
Diabetes mellitus ^f	17 (11.6)	15 (38.5)	10 (14.1)	1 (7.7)
<i>P</i> -value*	–	<0.0001	0.5966	0.6719
Dyslipidemia ^g	52 (35.4)	17 (43.6)	18 (25.4)	4 (30.8)
<i>P</i> -value*	–	0.3451	0.1375	0.7386

CLL, chronic lymphocytic leukemia; MedDRA, Medical Dictionary for Regulatory Activities; N/C, not calculated; PMH, past medical history; R/R, relapsed/refractory; SD, standard deviation; SMQ, Standardized MedDRA Query; y, years.

*Versus acalabrutinib monotherapy. *P*-values were not calculated when numbers were low.

^aPatients with R/R CLL from ELEVATE-RR.

^bPatients with CLL treated with obinutuzumab + chlorambucil (ELEVATE-TN), idelalisib + rituximab (ASCEND), or bendamustine + rituximab (ASCEND).

^cPMH of hypertension defined as MedDRA v25.1 (narrow) hypertension SMQ.

^dAmong patients whose smoking habits were collected.

^eAggregate term that includes the following terms: chronic kidney disease, dialysis device insertion, glomerulonephritis chronic, kidney fibrosis, and renal failure.

^fAggregate term that includes the following terms: diabetes mellitus, glucose tolerance impaired, glycosylated hemoglobin increased, hyperglycemia, impaired fasting glucose, insulin resistance, type 1 diabetes mellitus, and type 2 diabetes mellitus.

^gAggregate term that includes the following terms: blood cholesterol increased, diabetic dyslipidemia, dyslipidemia, hypercholesterolemia, hyperlipidemia, hypertriglyceridemia.