

Supplemental Table 1: CLL patients' characteristics and clinical treatment.

Patients	Sex	Age, yr	Rai stage	Lymph count x 10 ⁹ /l	WBC count x 10 ⁹ /l	IgVh mutation (%)	CD38 level (%)	del11 (ATM)	del17 (p53)	Clinical Treatment	Resistance to Clinical Treatment
CLL1	M	74	II	147.9	166.2	0.0	n.d.	no	no	U	N/A
CLL2	M	53	II	61.7	88.1	n.d.	n.d.	n.d.	n.d.	FCR	N/A
CLL3	M	66	IV	95.0	101.6	5.5	2.4	no	no	C, R	Yes
CLL4	M	80	III	40.6	61.5	0.8	36.5	n.d.	n.d.	U	N/A
CLL5	M	70	II	168.7	193.9	0.0	2.7	yes	no	U	N/A
CLL6	F	74	III	212.6	265.8	4.0	15.7	n.d.	n.d.	F, R	no
CLL7	M	88	n.d.	133.1	166.4	3.0	n.d.	n.d.	n.d.	F	yes
CLL8	F	91	II	60.9	98.3	5.3	27.3	n.d.	n.d.	C	no
CLL9	M	74	0	41.5	52.5	7.2	85	n.d.	n.d.	U	N/A
CLL10	F	67	III	41.2	47.4	4.0	41.1	n.d.	n.d.	C, F	no
CLL11	M	72	II	166.9	199.6	0.0	3.6	no	no	U	N/A
CLL12	F	75	0	73.8	104.0	3.8	n.d.	n.d.	n.d.	F, R	yes
CLL13	M	88	IV	83.7	95.1	0.0	85.1	n.d.	n.d.	C	yes
CLL14	M	68	I	39.9	49.3	4.5	10.4	n.d.	n.d.	U	N/A
CLL15	M	72	III	59.7	67.1	4.0	n.d.	n.d.	n.d.	U	N/A
CLL16	M	81	IV	68.1	74.0	11.2	n.d.	no	no	U	N/A
CLL17	M	83	IV	81.4	92.5	0.0	29.6	n.d.	n.d.	C	no
CLL18	M	71	II	55.4	67.5	0.0	22.2	yes	no	U	N/A
CLL19	F	70	IV	212.0	230.0	0.0	n.d.	yes	yes	CHOP	no
CLL20	F	90	n.d.	62.2	74.1	2.4	n.d.	n.d.	n.d.	U	N/A
CLL21	F	57	III	166.5	179.0	12.5	2	n.d.	n.d.	U	N/A
CLL22	F	53	II	79.0	94.0	0.0	n.d.	n.d.	n.d.	FCR	yes
CLL23	M	74	II	151.4	166.4	9.1	65.5	no	no	C	yes
CLL24	M	96	IV	118.8	129.1	9.4	n.d.	n.d.	n.d.	C	?
CLL25	F	55	n.d.	93.5	108.7	0.0	25.7	yes	no	U	N/A
CLL26	F	68	I	45.9	65.8	7.8	66.6	n.d.	n.d.	U	N/A
CLL27	F	78	II	70.6	106.9	8.0	32	no	no	U	N/A
CLL28	F	57	II	152.8	171.7	1.5	n.d.	no	yes	FCR, A	yes
CLL29	F	74	I	169.6	184.3	4.7	5.1	n.d.	n.d.	U	N/A
CLL30	M	70	II	90.9	93.2	11.4	2.7	no	no	C, F	yes
CLL31	M	64	I	65.3	73.4	9.9	4.9	no	no	U	N/A
CLL32	M	64	I	56.5	61.4	n.d.	n.d.	yes	no	F, A	yes
CLL33	M	67	IV	52.4	56.3	1.0	n.d.	no	no	FCR	no
CLL34	F	87	0	30.0	42.9	n.d.	n.d.	n.d.	n.d.	U	N/A
CLL35	F	71	II	112.9	128.3	7.0	4	no	yes	U	N/A
CLL36	F	47	IV	117.2	126.0	0.0	2.3	no	no	U	N/A
CLL37	F	94	n.d.	n.d.	n.d.	4.9	n.d.	n.d.	n.d.	U	N/A
CLL38	M	55	0	270.9	282.2	4.6	3	n.d.	n.d.	U	N/A

Patients	Sex	Age, yr	Rai stage	Lymph count x 10 ⁹ /l	WBC count x 10 ⁹ /l	IgVh mutation (%)	CD38 level (%)	del11 (ATM)	del17 (p53)	Clinical Treatment	Resistance to Clinical Treatment
CLL39	F	69	II	185.7	199.7	0.1	n.d.	no	no	C	no
CLL40	F	64	II	170.5	179.5	11.2	8.3	no	no	U	N/A
CLL41	M	70	0	126.3	135.8	0.0	n.d.	no	no	U	N/A
CLL42	F	77	II	150.6	165.5	0.0	n.d.	n.d.	n.d.	C	no
CLL43	M	72	III	178.4	191.8	7.2	n.d.	no	no	C	no
CLL44	M	77	0	68.6	77.2	n.d.	n.d.	n.d.	n.d.	U	N/A
CLL45	M	90	III	63.6	79.5	0.0	n.d.	n.d.	n.d.	C	?
CLL46	F	71	II	61.2	72.0	4.0	17	n.d.	n.d.	U	N/A
CLL47	F	78	II	77.1	92.5	6.3	3.4	no	no	U	N/A
CLL48	F	83	IV	84.9	141.5	0.0	18	no	no	C, F, R	yes
CLL49	F	79	0	28.2	38.1	n.d.	n.d.	n.d.	n.d.	U	N/A
CLL50	M	58	II	186.4	215.0	n.d.	n.d.	yes	no	FCR	yes
CLL51	M	78	IV	81.1	89.1	7.4	2.8	no	no	U	N/A
CLL52	M	45	0	83.9	91.0	5.2	5.2	no	no	U	N/A
CLL53	M	65	I	64.6	81.8	0.0	0	no	no	U	N/A
CLL54	M	85	III	47.8	59.7	0.0	0	n.d.	n.d.	U	N/A
CLL55	F	75	II	197.0	209.6	6.4	6.4	no	no	CLB	no
CLL56	M	81	0	90.6	116.2	0.0	n.d.	n.d.	n.d.	P	no
CLL57	F	61	IV	207.9	221.2	0.0	64.7	n.d.	n.d.	FCR,CHOP	yes
CLL58	M	69	II	77.6	94.6	0.0	9.5	no	no	FCR	no
CLL59	M	77	0	214.6	238.4	8.3	n.d.	no	no	U	N/A
CLL60	F	30	0	n.d.	n.d.	6.1	n.d.	n.d.	n.d.	n.d.	n.d.
CLL61	M	74	0	153.0	182.1	7.8	n.d.	no	no	C, FCR	yes
CLL62	M	89	I	80.4	84.6	9.8	2	no	no	U	N/A
CLL63	M	85	0	24.5	31.9	5.1	1.1	no	no	U	N/A
CLL64	M	58	II	58.8	68.4	0.0	16	no	no	U	N/A
CLL65	M	66	0	42.4	50.5	6.7	2.4	n.d.	n.d.	U	N/A

Summary of the clinical characteristics of 65 B-CLL patients that provided lymphocytes for this work. Rai classification separates CLL into low (stage 0), intermediate (stage I & II) and high (stage III& IV) risk categories. IgVH: Percentage of somatic mutations in the immunoglobulin variable region genes. WBC: white blood count, lymph: lymphocytes, A: Alemtuzumab, C: chlorambucil, F: fludarabine, P: prednisone, FCR: Fludarabine/Cyclophosphamide/Rituximab, CHOP: Cyclophosphamide/Hydroxyldaunorubicin/Oncovin/Prednisone, n.d.: not determined, N/A: Not Applicable.

Supplemental Table 2: BKM120 and Cal-101 IC₅₀s in B-CLL samples.

Patients	IC ₅₀ (μM)		Patients	IC ₅₀ (μM)	
	BKM120	Cal-101		BKM120	Cal-101
CLL1	0.3		CLL34	3.4	50.0
CLL2	0.4		CLL35	3.9	
CLL3	0.5	10.5	CLL36	4.7	50.0
CLL4	0.5		CLL37	4.8	
CLL5	0.5		CLL38	4.8	
CLL6	0.6	2.5	CLL39	5.0	22.4
CLL7	0.6		CLL40	5.3	
CLL8	0.6		CLL41	5.4	
CLL9	0.7		CLL42	7.1	
CLL10	0.8		CLL43	8.3	50.0
CLL11	0.8		CLL44	9.1	
CLL12	0.9		CLL45	9.5	
CLL13	1.0		CLL46	12.3	
CLL14	1.0		CLL47	12.3	
CLL15	1.3		CLL48	12.4	50.0
CLL16	1.4		CLL49	13.2	50.0
CLL17	1.4	50.0	CLL50	19.2	50.0
CLL18	1.6		CLL51	19.2	
CLL19	1.7	3.1	CLL52	20.0	
CLL20	1.8	6.4	CLL53	20.0	11.4
CLL21	1.8		CLL54	20.0	
CLL22	1.8		CLL55	20.0	
CLL23	1.9	50.0	CLL56	20.0	
CLL24	2.2	50.0	CLL57	20.0	3.8
CLL25	2.4		CLL58	20.0	
CLL26	2.5		CLL59	20.0	
CLL27	2.8		CLL60	20.0	
CLL28	2.8		CLL61	20.0	50.0
CLL29	2.9		CLL62	20.0	50.0
CLL30	2.9		CLL63	20.0	
CLL31	3.1		CLL64	20.0	
CLL32	3.3		CLL65	20.0	25.8
CLL33	3.4	5.7			

The MTT assay was used to determine the BKM120 IC₅₀ (65 samples) and Cal-101 IC₅₀ (20 samples) in B-lymphocytes isolated from B-CLL patients.

Supplemental Table 3: Statistics for the CLL patients population involved in this study.

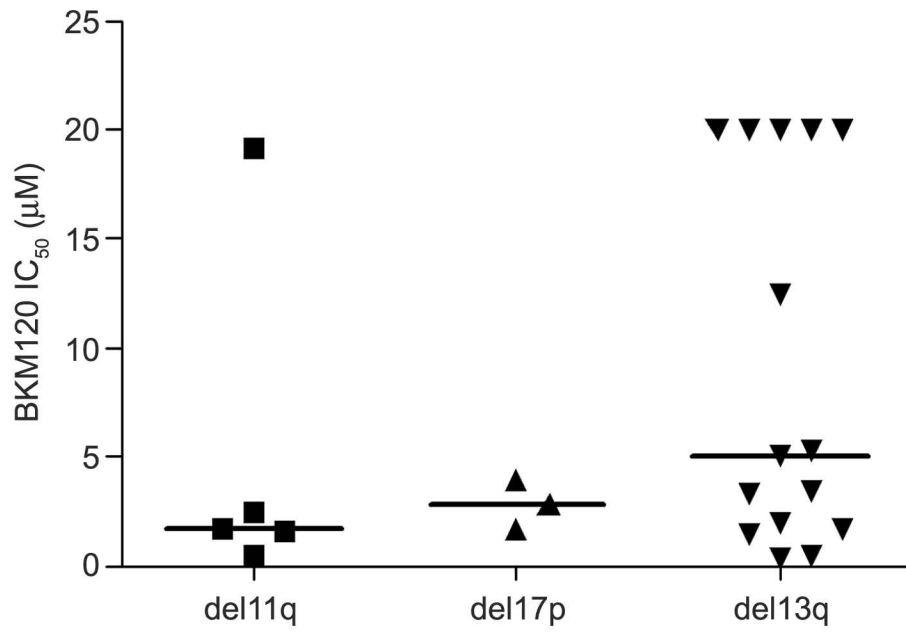
		# of patients	% of patients
Age	>65ans	50	77%
	<45ans	2	3%
	median	72	N/A
	range (Years)	30-96	N/A
Sex		# of patients	% of patients
	F	27	42%
	M	38	58%
	ratio M:F	1.4:1	N/A
Rai stage (61 patients tested)	Stage	# of patients	% of patients
	0	14	23%
	I	7	11%
	II	21	34%
	III	8	13%
	IV	11	18%
	n.d	4	N/A
IgVh mutation (%) (59 patients tested)	Status	# of patients	% of patients tested
	unmutated	24	41%
	mutated	35	59%
	n.d	6	N/A
CD38 level (%) (38 patients tested)	Status	# of patients	% of patients tested
	negative	30	79%
	positive	8	21%
	n.d	27	N/A
Cytogenetic deletions	# tested	# positive	% of patients tested
none	32	6	16%
del11q	32	6	19%
del17p	32	3	9%
del13q	26	15	58%
Clinical Treatment	treatment	# of patients	% of patients tested
	untreated	36	56%
	treated	28	44%
Resistance to Clinical Treatment (15 patients tested)	resistance	# of patients	% of patients tested
	yes	13	48%
	no	12	44%
	n.d	2	N/A

n.d.: not determined, N/A: Not Applicable.

The percentages observed for the characteristic markers in our cohort of CLL patients are representative of the CLL population in general¹⁻⁵.

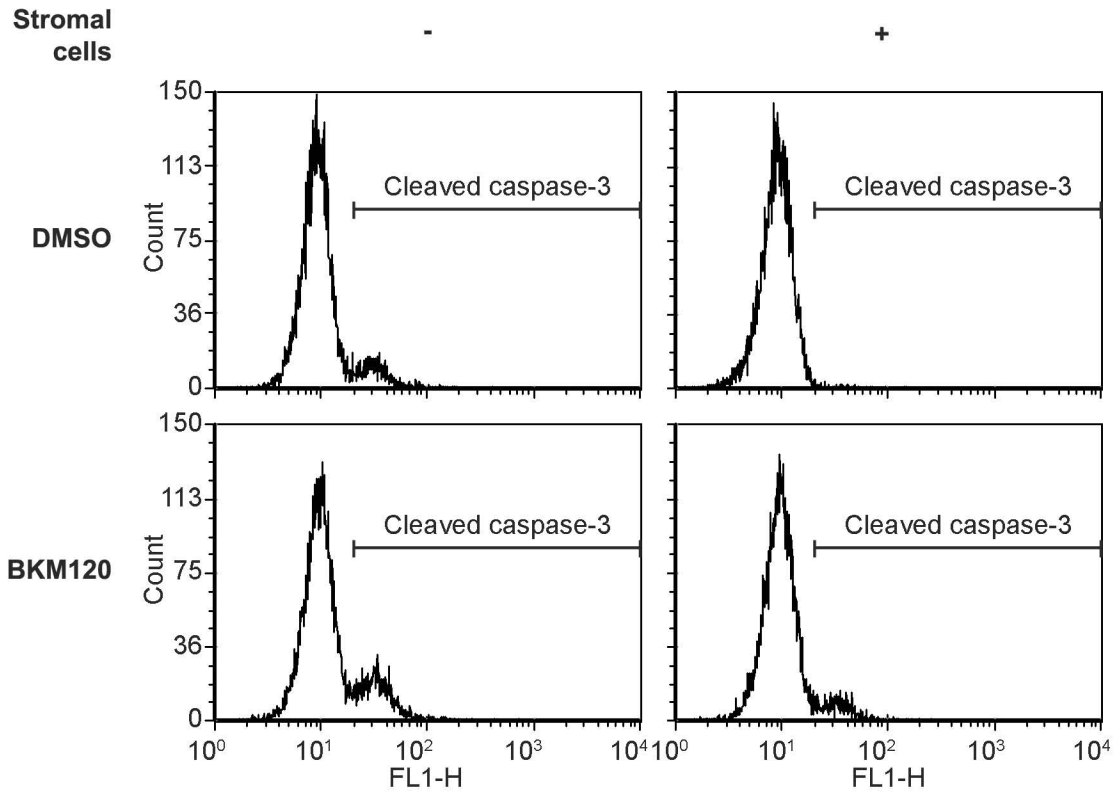
References for supplemental Table 3:

1. Oscier DG, Gardiner AC, Mould SJ, Glide S, Davis ZA, Ibbotson RE, Corcoran MM, Chapman RM, Thomas PW, Copplestone JA, Orchard JA, Hamblin TJ. Multivariate analysis of prognostic factors in CLL: clinical stage, IGVH gene mutational status, and loss or mutation of the p53 gene are independent prognostic factors. *Blood* 2002;100:1177-84.
2. Cramer P, Hallek M. Prognostic factors in chronic lymphocytic leukemia-what do we need to know? *Nat Rev Clin Oncol* 2011;8:38-47.
3. Shanshal M, Haddad RY. Chronic lymphocytic leukemia. *Dis Mon* 2012;58:153-67.
4. Clifford R, Schuh A. State-of-the-Art Management of Patients Suffering from Chronic Lymphocytic Leukemia. *Clin Med Insights Oncol* 2012;6:165-78.
5. Sellner L, Dietrich S, Dreger P, Glimm H, Zenz T. Can prognostic factors be used to direct therapy in chronic lymphocytic leukemia? *Curr Hematol Malig Rep* 2012;7:3-12.



Supplemental Figure 1

A



B

