Clinical significance of bax/bcl-2 ratio in chronic lymphocytic leukemia

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Table 1S. Distribution of prognostic factors in the validation cohort of CLL (n=233 pts) according to bax/bcl-2 values

	bax/bcl-2, no							
Parameter	**≥1.50**	**<1.50**	**P¶**	**n§**	**10-year OS,%**	**P***	**10-year PFS, %**	**P***
Age								
<60 years	42	46	0.34	233	93	0.00005	21	0.78
>60 years	64	81			70		22	
B_2M								
<2.2 g/L	79	44	<0.0001	233	94	<0.0001	40	<0.0001
>2.2 g/L	27	83			61		3	
Mod-Rai								
I	43	23	0.0002	233	89	0.01	39	<0.0001
II-III	63	104			77		16	
sCD23								
<70 UI/ml	77	40	<0.0001	204	94	<0.0001	40	<0.0001
>70 UI/ml	16	71			62		3	
CD38								
<30%	86	81	0.003	233	84	0.0009	31	<0.0001
>30%	20	46			67		3	
FISH								
Normal/del13q	88	62	<0.0001	231	91	<0.0001	32	<0.0001
Int/Poor (+12, del11q, del17p)	17	64			59		3	
IGHV								
M	85	52	<0.0001	232	94	<0.0001	34	<0.0001
UM	20	75			57		5	
TP53								
M	1	18	0.0001	233	83	0.00002	8	0.006
WT	105	109			45		31	
NOTCH-1								
M	4	35	<0.0001	233	85	<0.0001	0	0.00002
WT	102	92			42		27	

¶ Fisher exact tests were performed to evaluate the association between bax/bcl-2 values (below or above the established threshold set at ≥1.50 of positive CLL cells) and other prognostic factors. § Values refer to the number of cases analyzed for a given feature. * P values were calculated by the log-rank test.
+ At 8 years.

Table 2S. Comparison between the same patients with regard to bax/bcl-2 ratio (LAB1: anti-bax unconjugated MoAb and LAB2: anti-bax APC MoAb)

	LAB1 (fresh cells) Bax/bcl-2	LAB2 (thawed cells) Bax/bcl-2
R.G.	0.5	1.16
B.S.	0.51	1.35
S.G.	0.52	1.25
M.M.P.	0.55	1.31
T.A.	0.57	0.99
D.G.R.	0.58	1.27
C.A.I	0.59	1.27
G.V.	0.62	1.41
G.G.	0.74	1.30
F.M.	1.07	1.03
D.M.	1.5	0.88
M.S.	1.77	2.20
D.A.G.	1.79	2.31
T.S.	1.8	4.76
L.A.	1.84	2.68
P.B.	1.89	1.69
S.L.	1.93	2.20
P.A.	1.94	4.13
F.L.	3.5	5.67
D.M.G.	5.22	4.14

Spearman correlation

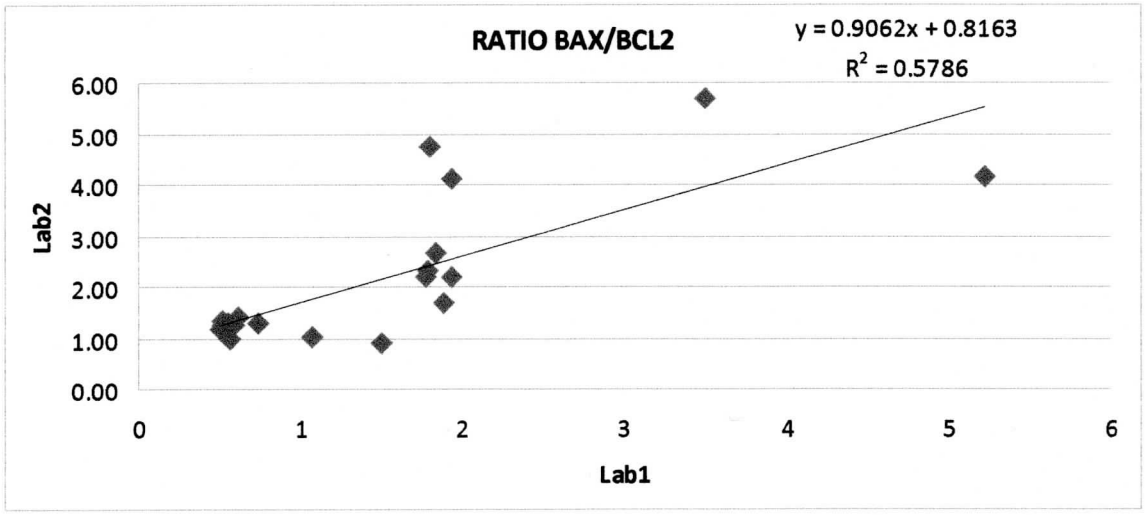


Table 3S. Prognostic factors in CLL according to bax/bcl-2 ratio in 52 cases (CLL subset analysed using anti-bax FITC)

	bax/bcl-2, no			
Parameter	**≥1.50**	**<1.50**	**P¶**	**n§**
Age				
<60 years	12	12	0.50	52
>60 years	13	15		
B_2M				
<2.2 g/L	21	7	0.00003	52
>2.2 g/L	4	20		
Mod-Rai				
I	14	2	0.0002	52
II-III	11	25		
sCD23				
<70 UI/ml	20	7	<0.0001	47
>70 UI/ml	1	19		
CD38				
<30%	24	19	0.025	52
>30%	1	8		
FISH				
Normal/del13q	24	13	0.0001	52
Int/Poor (+12, del11q, del17p)	1	14		
IGHV				
M	24	6	<0.0001	52
UM	1	21		
TP53				
M	0	8	0.004	52
WT	25	19		
NOTCH-1				
M	1	8	0.025	52
WT	24	19		

¶ Fisher exact tests were performed to evaluate the association between bax/bcl-2 values (below or above the established threshold set at ≥1.20 of positive CLL cells) and other prognostic factors. § Values refer to the number of cases analyzed for a given feature. * P values were calculated by the log-rank test.

Table 4S. Bax/bcl-2 values along the course of the disease in 46 untreated CLL patients.

Patient ID	Basal bax/bcl-2	Bax/bcl-2 after 1 year	Bax/bcl-2 after 2 years
A.L.	2.41	2.16	2.09
A.G	2.78	3.11	2.85
A.L.G	1.11	0.97	1.12
B.M.T.	0.82	0.75	0.83
B.F.	0.84	0.91	1.01
B.A.	1.83	2.01	1.92
C.P.	3.81	3.44	3.62
C.D.	0.57	0.68	0.72
C.M.	2.14	2.22	2.01
C.G.	0.87	0.77	0.91
C.E.	2.94	2.54	2.33
C.G.	0.44	0.51	0.58
D.G.	1.80	1.84	1.76
D.B.D.	0.69	0.75	0.79
D.L.A.	2.37	2.18	2.44
D.C.G.	1.00	1.08	1.12
D.M.G.	5.22	4.89	4.76
D.M.T	0.85	0.64	0.78
E.G.	1.09	1.05	1.11
F.E.	2.52	2.79	2.41
F.L.	3.11	3.01	2.92
F.M.	1.07	0.99	1.10
G.G.	1.89	2.12	2.31
I.F.	0.27	0.35	0.38
L.A.	2.38	2.21	2.61
L.F.	0.50	0.61	0.39
M.V.	1.03	1.15	0.86
M.C.	6.03	5.55	5.83
M.F.	0.11	0.19	0.24
N.G.	1.81	2.02	2.05
N.D.	1.12	1.23	1.08
O.C.	0.86	1.03	0.79
P.M.A.	2.40	2.62	2.35
P.G.	1.42	1.24	1.08
R.I.	1.29	0.98	0.56
R.G.	1.59	1.75	1.90
R.M.	2.22	2.12	2.01
S.G.	0.52	0.66	0.41
S.M.	2.42	2.31	2.25
S.A.	0.46	0.58	0.66
S.L.	1.21	1.15	0.97
T.A.	0.73	0.69	0.54
T.C.	2.31	2.10	2.08
T.A.	1.69	1.82	1.86
V.L.	1.89	2.13	2.02
Z.G.	0.87	0.61	0.53

Legend to Supplemental Figures

Figure 1S. Receiver-operating characteristic (ROC) analysis. Bax/bcl-2 ratio cut-off yelding the best separation of 2 subgroups with different OS and/or PFS probabilities obtained by ROC analysis was ≥ 1.42 with only 10 cases inconsistent with bax/bcl-2 ratio median value (≥ 1.50).

Figure 2S. Progression-free survival (PFS) and overall survival (OS) curves based on bax/bcl-2 values in the validation CLL cohort. Kaplan-Meier plot comparing PFS (A) and OS (B) based on the detection of bax/bcl-2 ratio ≥1.50 (bax/bcl2+) or <1.50 (bax/bcl2-). Bax/bcl2+ patients experienced both a longer PFS and OS ($p<0.0001$).

Figure 1S

Cut-off <= 1,4229

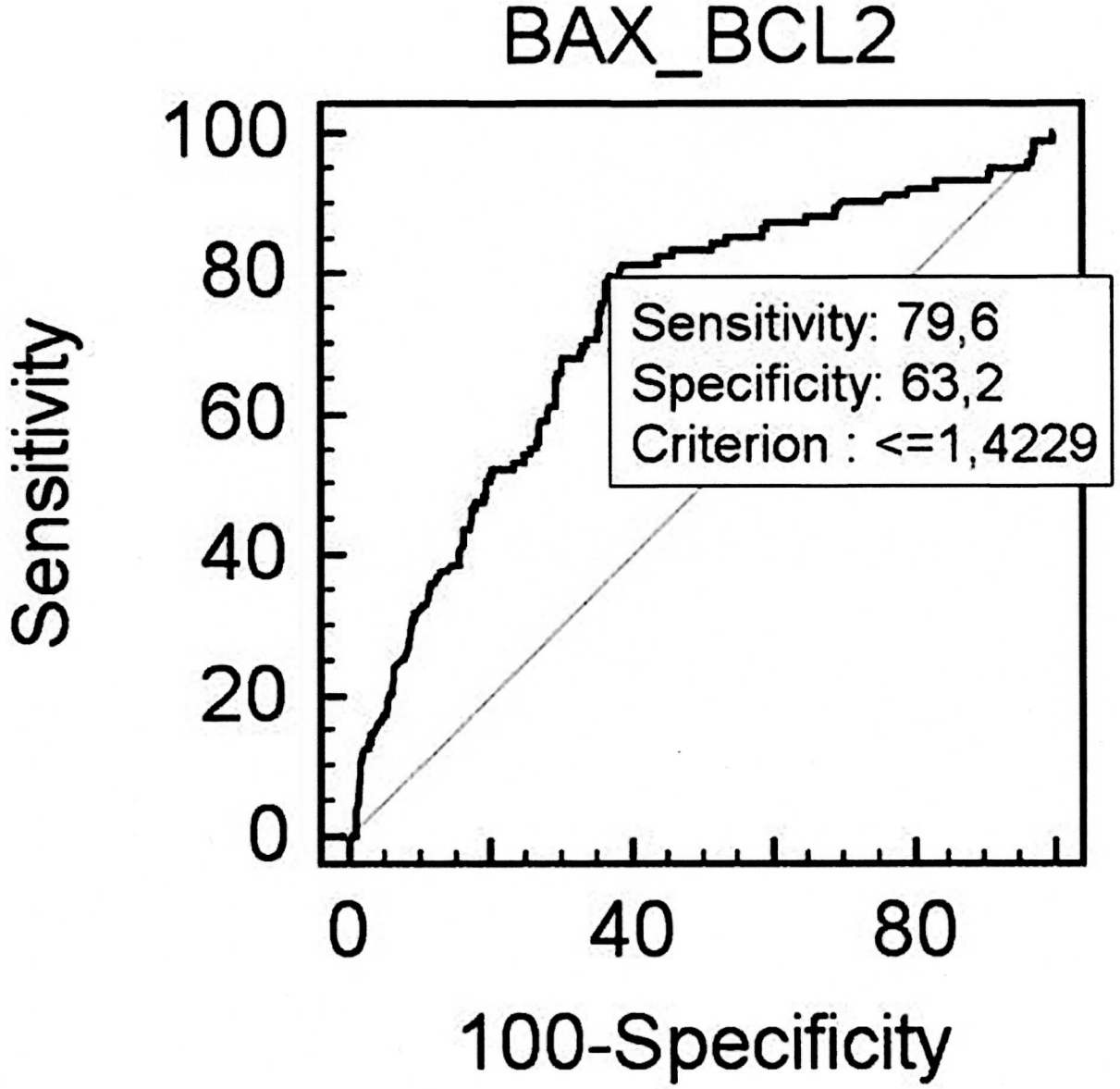
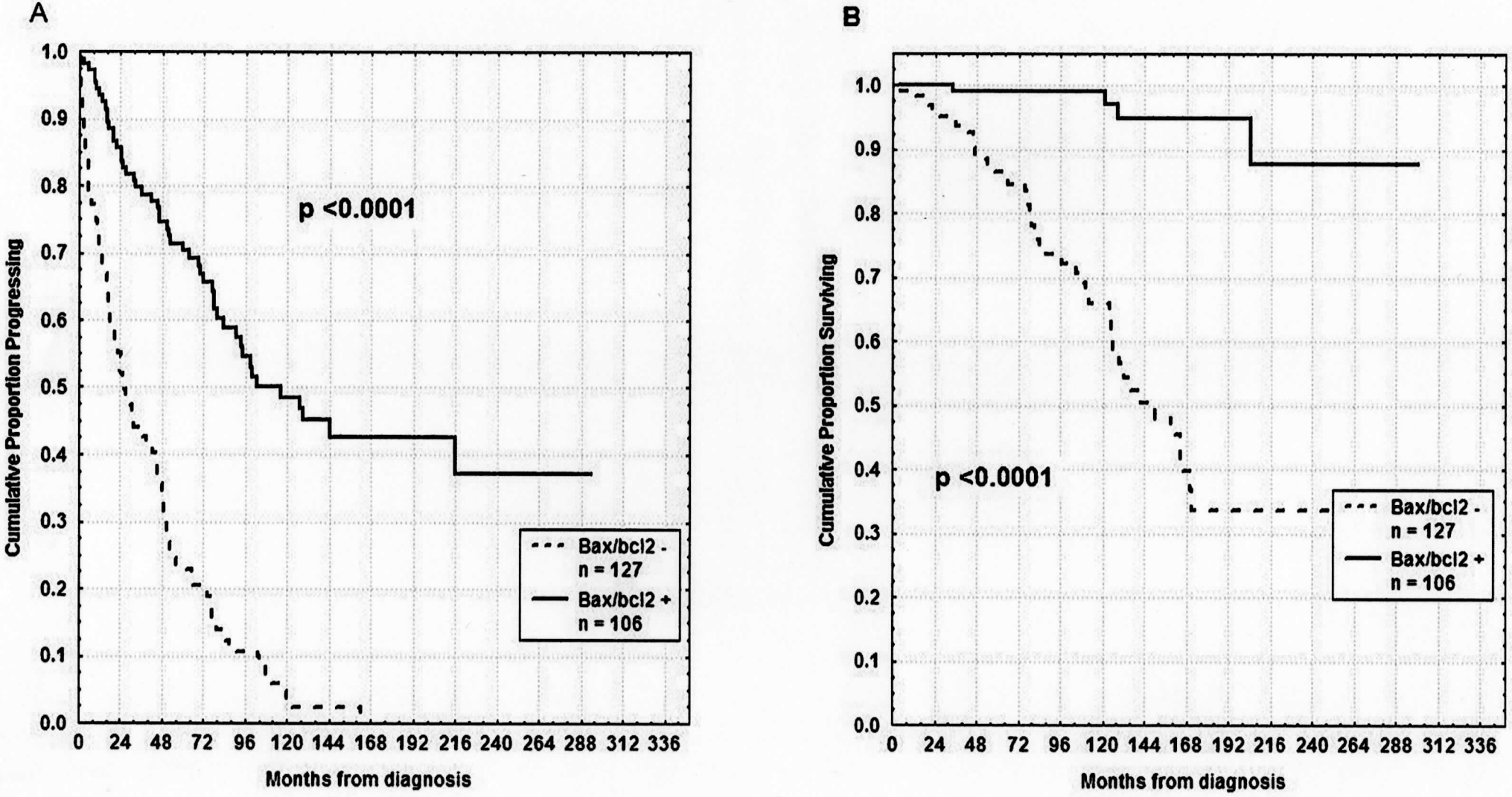


Figure 2S


A
Cumulative Proportion Progressing
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
p <0.0001
Bax/bcl2 -
n = 127
Bax/bcl2 +
n = 106
0 24 48 72 96 120 144 168 192 216 240 264 288 312 336
Months from diagnosis
B
Cumulative Proportion Surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
p <0.0001
Bax/bcl2 -
n = 127
Bax/bcl2 +
n = 106
0 24 48 72 96 120 144 168 192 216 240 264 288 312 336
Months from diagnosis