SUPPLEMENTARY INFORMATION

Univariate and multivariate analyses

We analyzed the association of the prognostic factors of each index with OS, as well as the HR of the univariate and multivariate analyses.

Regarding the univariate analysis of the sample used for the validation of the MDACC index, significance was shown for age, β2-microglobulin, absolute lymphocyte count, number of nodal regions affected and Rai stage. In the sex variable, a trend close to statistical significance was observed (p = 0.0067). However, in the multivariate analysis, significance was shown for sex but not for absolute lymphocyte count (p = 0.111). The factor that showed the greatest impact in the multivariate analysis was the pooling of patients in 0/I/II Rai stage *vs* III/IV Rai stage (HR = 3.1). A more comprehensive explanation of these analysis can be observed in Table S1.

Table S1. Univariate and multivariate Cox regression analysis of the variables included

in the MDACC score.

	Median OS (months) (CI 95%)	P	Univariate Cox regression HR (CI 95%)	P	Multivariate Cox regression HR (CI 95%)	P
Age (years)						
<50	238.5 (0-477.1)	0.007	1.055 (1.032-1.078) *for 1 year increase*	<0.0001	1.061 (1.035-1.086)	<0.0001
50-65	173.2 (NE)					
>65	142 (111.1-172.8)					
Sex						
Male	147.3 (111-183.6)	0.067	1.521 (0.971-2.385)	0.069	1.636 (1.016-2.636)	0.043
Female	194.5 (126.5-262.5)		1 (ref)			
β2-microglobulin (mg/L)						
Normal	238.5 (NE)	<0.0001	1.276 (1.209-1.346) *for 1mg/dL increase*	<0.0001	1.137 (1.055-1.225)	0.001
1-2 x ULN	143.5 (102.2-184.8)					
>2 x ULN	63.5 (NE)					
Lymphocyte count (x10^9/L)						
<20	194.5 (137.3-251.8)	<0.0001	1.004 (1.002-1.006) *for 1x10^9 increase*	<0.0001	1.002 (1.000-1.005)	0.111
20-50	143.5 (63-224.1)					
>50	76.2 (44.9-107.5)					
Enlarged node regions						
≤2	194.5 (148.9-240.2)	<0.0001	1 (ref)	<0.0001	2.454 (1.396-4.313)	0.002
>2	73.9 (62.6-85.2)		3.700 (2.333-5.868)			
Rai staging system						
0-2	194.5 (145-244)	<0.0001	1 (ref)	<0.0001	3.108 (1.471-6.566)	0.003
3-4	71.5 (23.2-119.7)		5.770 (3.205-10.389)			

OS, overall survival; CI95%, 95% confidence interval; HR, hazard ratio; NE, not evaluable; ULN, upper

limit normal; MDACC: MD Anderson Cancer Center.

In the univariate analysis of the CLL-IPI sample, β2-microglobulin, 17p-, *IGHV* mutational state, Rai stage and Binet stage were statistically significant. Only the comparison between patients ≤65 vs>65 years old did not obtain statistical significance (p = 0.171). However, in the multivariate analysis, no association between β2-microglobulin and OS (p = 0.268) was observed, but there was association when age was quantitatively analyzed. The factor with the greatest impact was 17p- (HR = 9.396). Details of these analyses can be seen in Table S2.

Table S2. Univariate and multivariate Cox regression analysis of the variables included
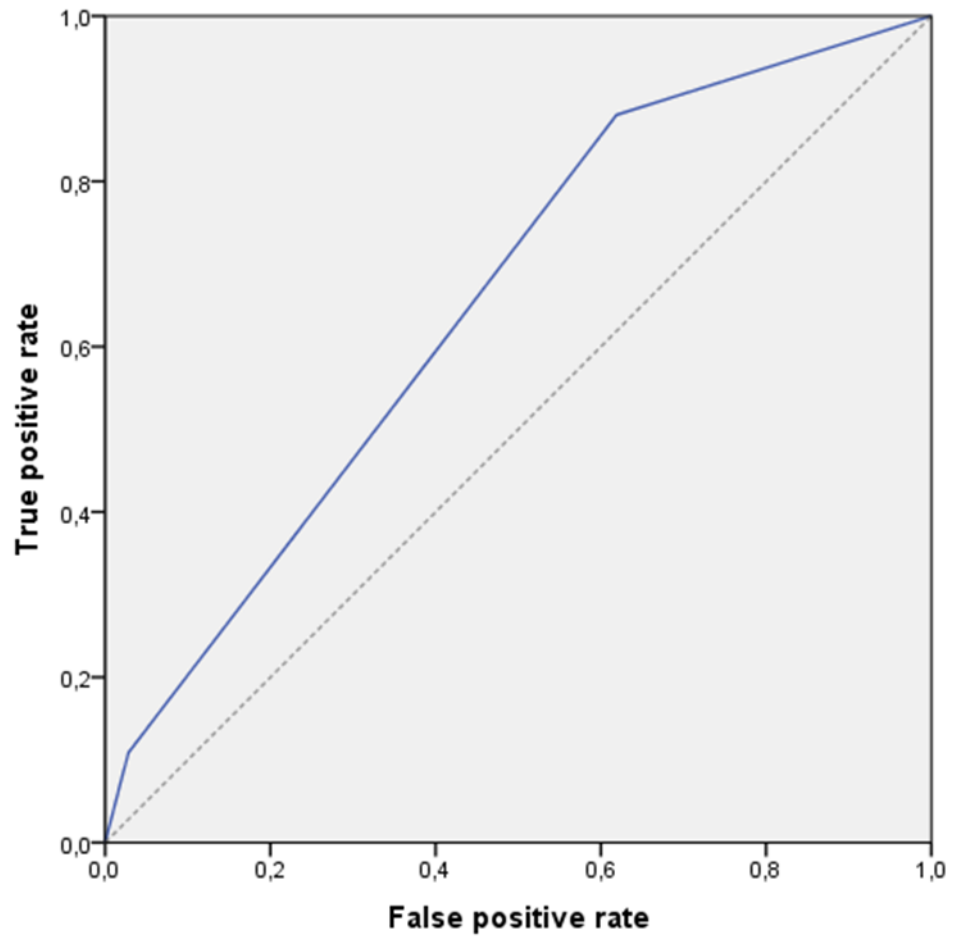
in the CLL-IPI score.

	Median OS (months) (CI 95%)	P	Univariate Cox regression		Multivariate Cox regression	
			HR (CI 95%)	P	HR (CI 95%)	P
Age (years)						
<65	238.5 (126.4-350.6)	0.171	1.031 (1.003-1.059)	0.028	1.047 (1.016-1.078)	0.003
≥65	Not reached		*for 1 year increase*			
β2-microglobulin (mg/L)				<0.0001 (n=237)	1.133 (0.909-1.412)	0.268
≤ 3.5	238.5 (129.9-347.2)	<0.0001	1.510 (1.273-1.791)			
>3.5	71.5 (58.1-84.8´9		*for 1mg/dL increase*			
Del 17p-						
Yes	31.8 (23.5-40.0)	<0.0001	11.478 (4.087-32.236)	<0.0001	9.396 (3.159-27.943)	<0.0001
Not	238.5 (129.4-347.6)		1 (ref)			
IGHV **mutation status**						
Mutated	238.5 (146.8-330.2)	<0.0001	1 (ref)	<0.0001	2.066 (1.003-4.136)	0.040
Non-mutated	131.9 (92.4-171.4)		3.141 (1.740-5.673)			
Rai staging system						
0	Not reached	<0.0001	1 (ref)	<0.0001	5.256 (2.541-11.288)	<0.0001
1-2	105.8 (31.8-179.8)		5.909 (3.080-11.337)			
3-4	71.5 (NE)		9.038 (2.995-27.274)			

OS, overall survival; CI95%, 95% confidence interval; HR, hazard ratio; NE, not evaluable; ULN, upper

limit normal; CLL-IPI: Chronic Lymphocytic Leukemia International Prognostic Index.

Figure S1. ROC curve for MDACC PI. (A) Overall Survival. (B) Time to First Therapy.
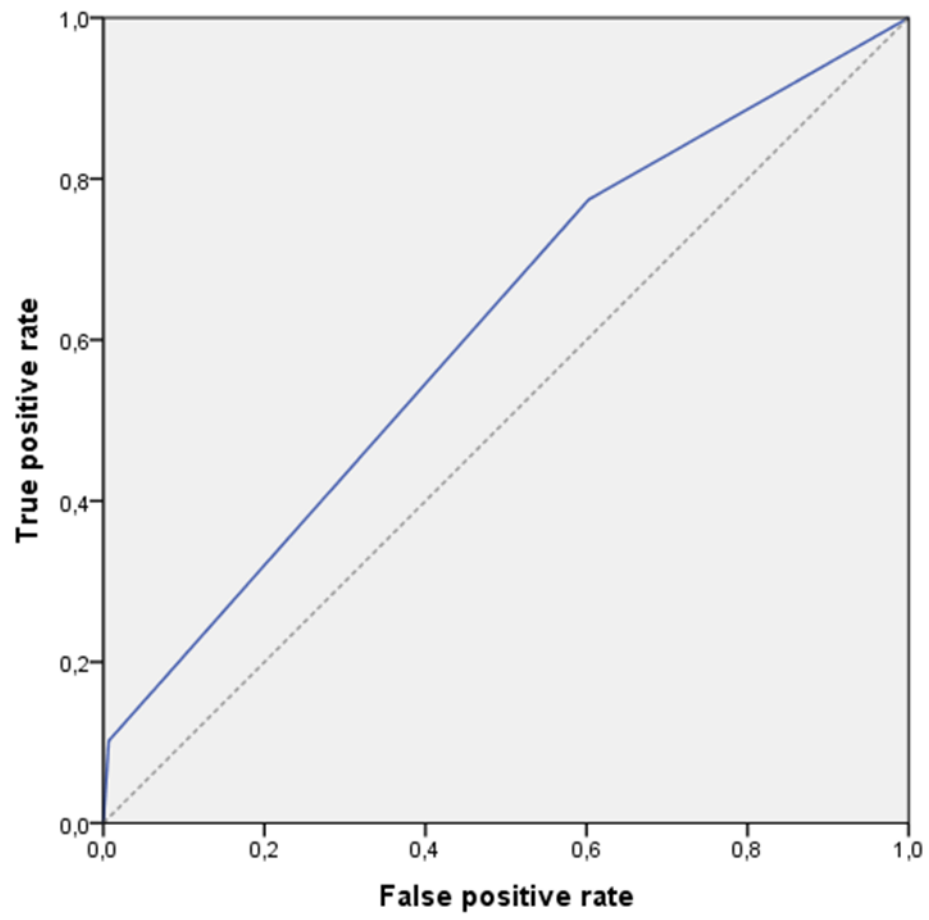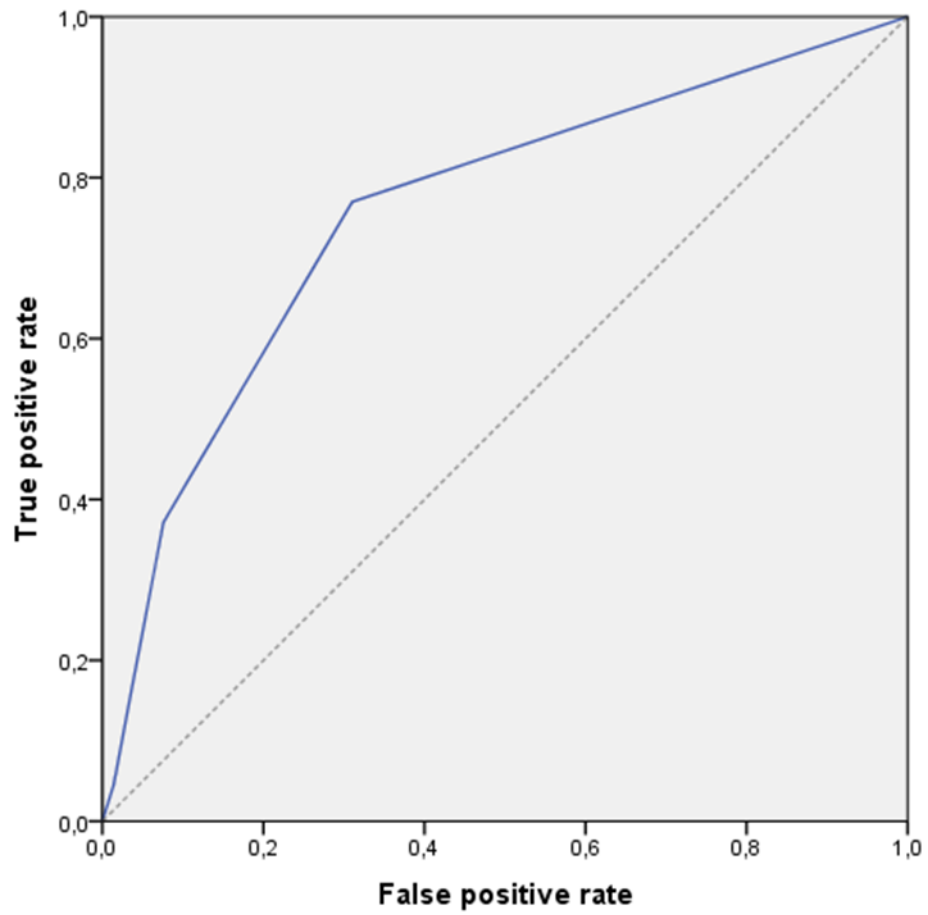
(A)

(B)

Figure S2. ROC curve for CLL-IPI. (A) Overall Survival. (B) Time to First Therapy.
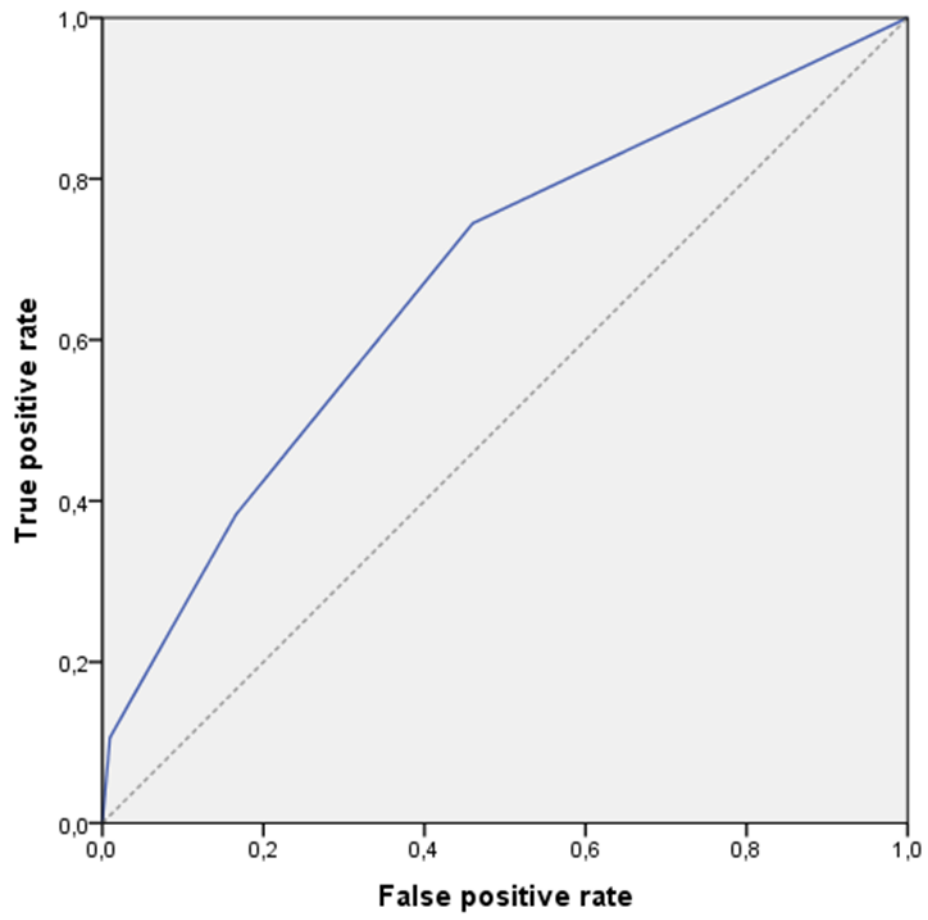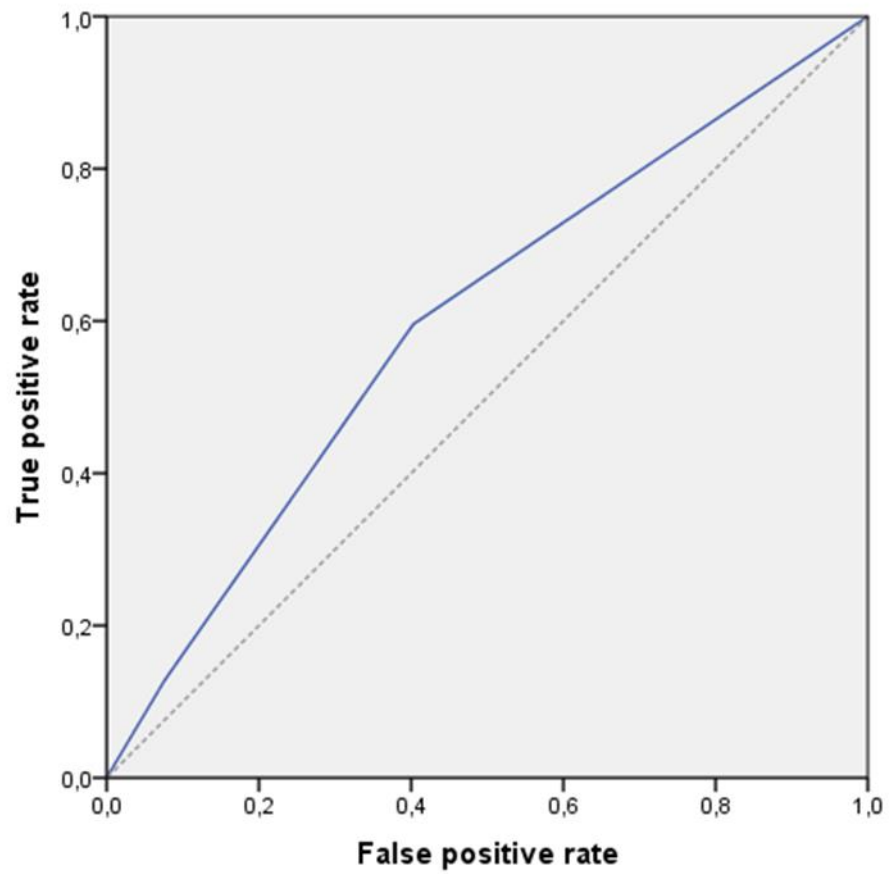
(A)

(B)

Figure S3. ROC curve for Barcelona-Brno biomarkers only prognostic model. (A) Overall Survival. (B) Time to First Therapy.

(A)

(B)