Supplementary statistical methods

Best cut-point selection was based on cubic regression splines representing the modeled transformed outcome (log HR in blue in Supplementary Figure 1) as a function of a covariate. When a steep increase or decrease of the log HR was observed in an area where the 95% CI (in red) was narrow, the nearest threshold value located in a flat zone was selected (e.g. age or number of nodal sites). When no such inflexion was observed (e.g. hemoglobin level or platelet count) or when the inflexion was near a usual cut-off (e.g. albumin), previously used cut-points were kept. For ß$_2$m where no inflexion was observed, both the UNL and the 3mg/L cut-off (used as a high tumor GELF criterion is some previous studies) were tested.

For Net Reclassification Improvement (NRI), a 5-yr time horizon and the continuous NRI were used. The overall NRI was reported in Table 3. The SAS macros from Professor Nancy Cook were used for NRI computation (http://ncook.bwh.harvard.edu/sas-macros.html).

For computing the Concordance Probability Estimates (CPE), we used the macro developed by Mithat Gönen, Qianxing Mo and Glenn Heller for SAS (http://support.sas.com/publishing/bbu/60610/SASphcpe.zip).

Supplementary Table 1. Patient characteristics in the validation set

	FL2000 (N=175)	MER (N=304)	All (N=479)
	N (%)	N (%)	N (%)
Age > 60 yrs	89 (51)	136 (45)	225 (47)
Male sex	96 (55)	165 (54)	261 (54)
ECOG > 1	11 (6)	13 (4)	24 (5)
Stage III-IV	152 (87)	236 (79)	388 (81)
Nodal sites involvement > 4	86 (49)	125 (44)	211 (44)
Bone marrow involvement	108 (62)	130 (46)	238 (50)
Extranodal sites involvement (other than bone marrow)	69 (40)	100 (33)	169 (35)
LDH > UNL	64 (37)	75 (27)	139 (29)
Hemoglobin < 12 g/dL	37 (21)	54 (19)	91 (19)
ß$_2$m > 3 mg/L	62 (38)	101 (33)	163 (34)
Induction treatment			
R-CHOP	0 (0)	121 (40)	121 (25)
R-CVP	0 (0)	68 (22)	68 (14)
R-bendamustine	0 (0)	104 (34)	104 (22)
R-CHVP+IFN	175 (100)	0 (0)	175 (37)
Others	0 (0)	11 (4)	11 (2)
Maintenance§			
Rituximab	0 (0)	95 (31)	95 (20)
IFN	175 (100)	0 (0)	175 (36)
None	0 (0)	209 (69)	209 (44)

Missing data: for the FL2000 cohort: ß2m (n=11), bone marrow involvement (n=1), LDH (n=4), stage (n=1), extranodal sites (n=3); for the MER cohort: ECOG (n=4), stage (n=7), nodal sites (n=21), bone marrow involvement (n=23), extranodal sites (n=6), LDH (n=22), hemoglobin (n=16).

Supplementary Table 2. Event-free survival at 24 months (EFS24) according to the PRIMA-PI or the FLIPI in the PRIMA cohort.

	FLIPI, n (%)		*Statistics*	PRIMA-PI, n (%)		*Statistics*
	Achieved EFS24	**Failed to achieve EFS24**		**Achieved EFS24**	**Failed to achieve EFS24**	
Low	200 (84)	38 (16)	**χ^2=22.27** **Φ_c=0.14** ***P*=1.36*10^{-5}**	303 (86)	49 (14)	**χ^2=55.48** **Φ_c=0.23** ***P*=1.41*10^{-12}**
Intermediate	319 (79)	86 (21)		272 (79)	74 (21)	
High	337 (69)	150 (31)		203 (62)	124 (38)	
Total	856 (76)	274 (24)		778 (76)	247 (24)	

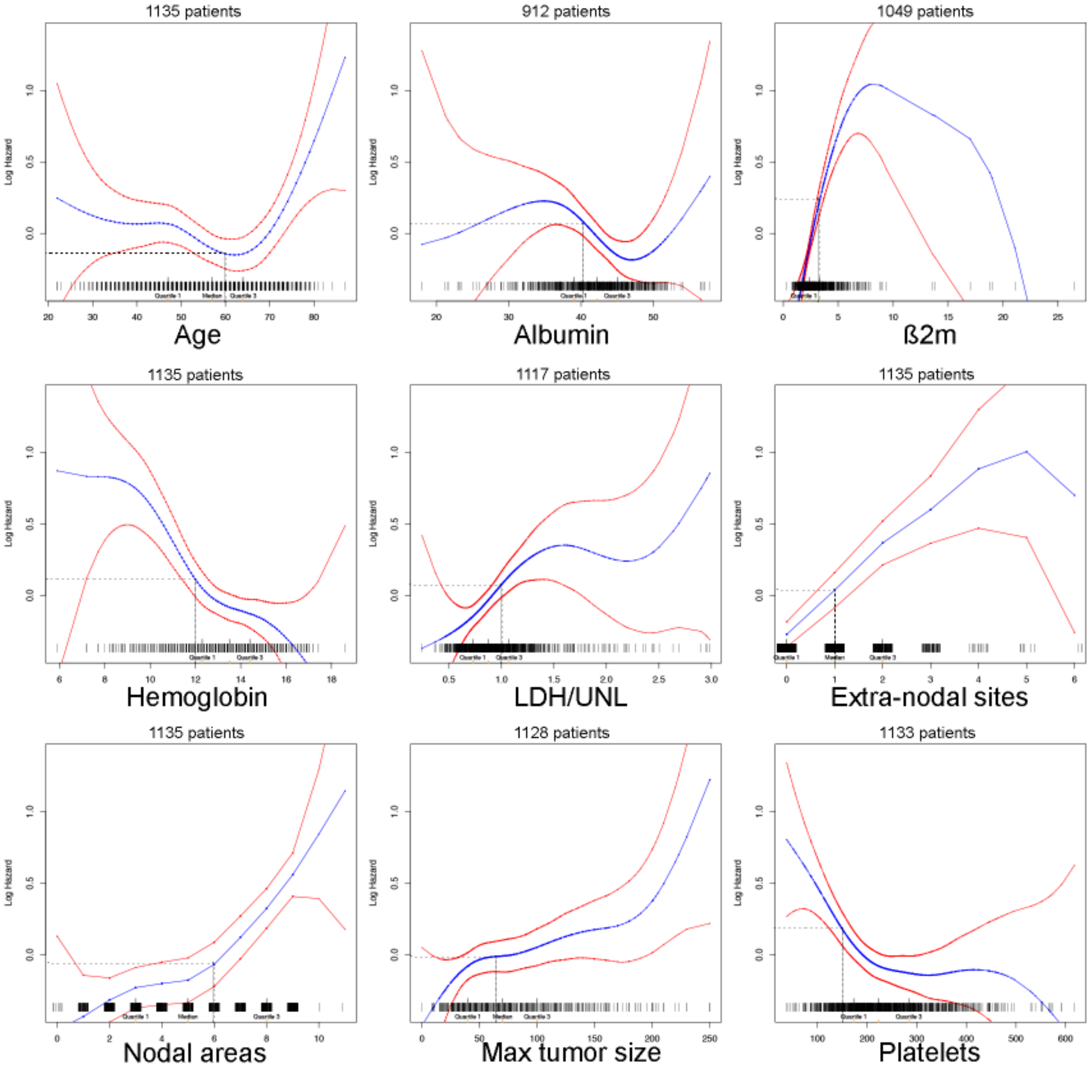
Φ_c=Cramer's V, P is calculated from the Fisher's exact test.

Supplementary Table 3. Event-free survival at 24 months (EFS24) according to the PRIMA-PI or the FLIPI in the validation cohort.

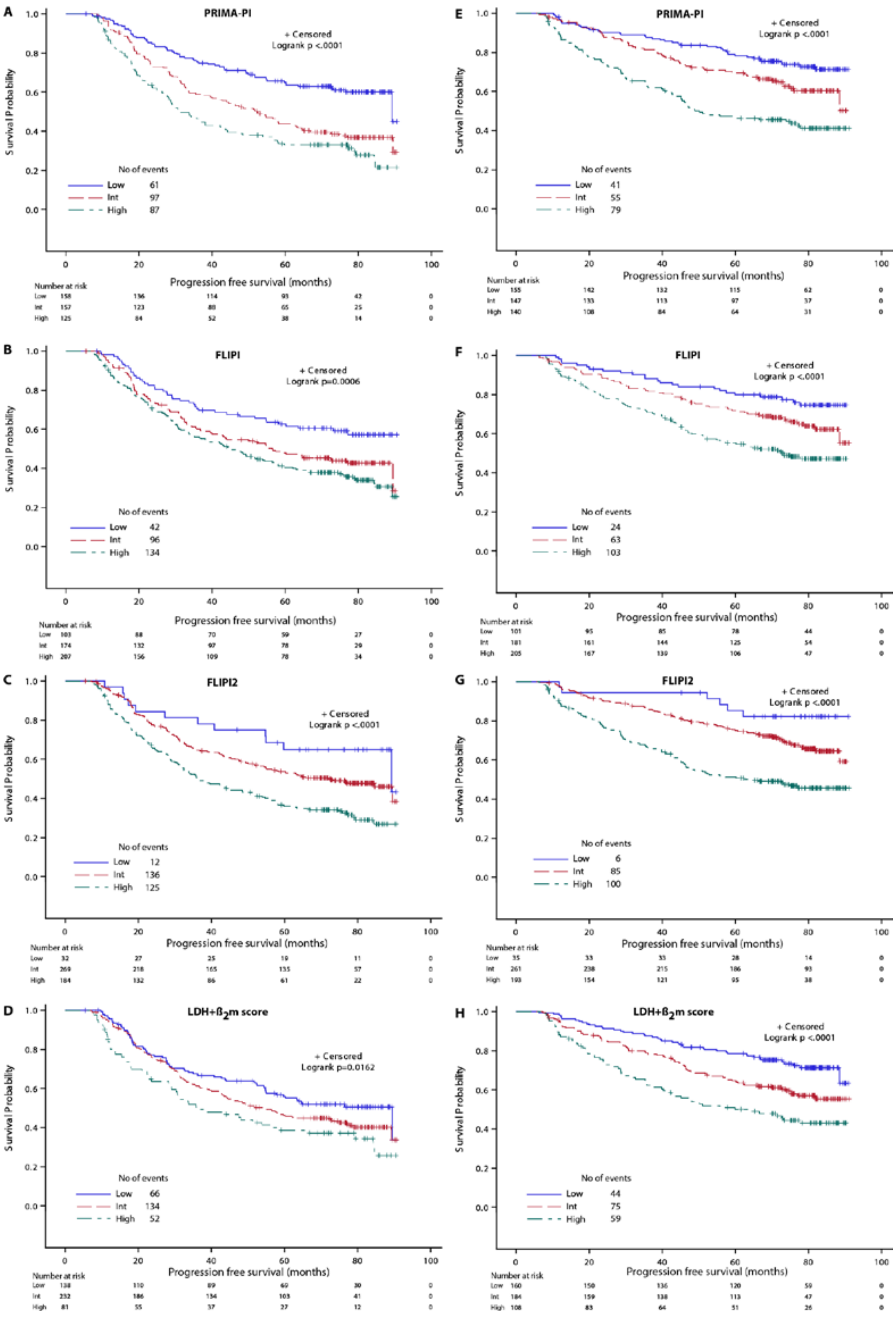
	FLIPI, n (%)		*Statistics*	PRIMA-PI, n (%)		*Statistics*
	EFS24-	**EFS24+**		**EFS24-**	**EFS24+**	
Low	112 (89)	14 (11)	**χ^2=13.21** **Φ_c=0.17** ***P*=0.0016**	151 (90)	17 (10)	**χ^2=18.24** **Φ_c =0.20** ***P*=0.0001**
Intermediate	133 (84)	26 (16)		112 (82)	24 (18)	
High	120 (73)	45 (27)		113 (72)	45 (28)	
Total	365 (81)	85 (19)		376 (81)	86 (19)	

Φ_c=Cramer's V, P is calculated from the Fisher's exact test.

Supplementary Figure 1. Cox regression splines analysis for best cut-off determination of continuous parameters.



Supplementary Figure 2. (A-D) PFS according to the four scores in the observation arm of the PRIMA study. (E-H) PFS according to the four scores in the rituximab maintenance arm of the PRIMA study.



Supplementary Figure 3. Survival in the training cohort. (A) OS according to the PRIMA-PI. (B) OS according to the FLIPI. (C) Lymphoma-specific survival according to the PRIMA-PI. (D) Lymphoma-specific survival according to the FLIPI.