Are there clinically relevant prognostic factors in diffuse large B-cell lymphoma beyond International Prognostic Index?

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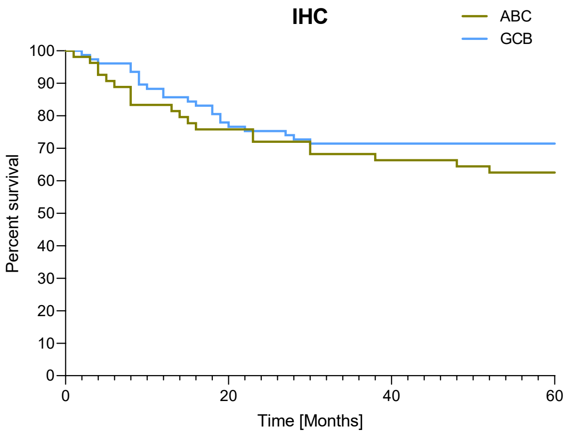
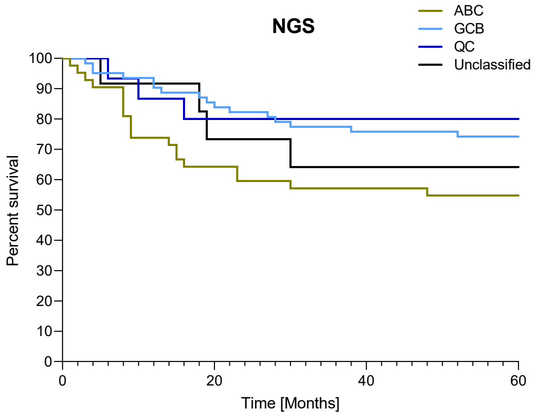


Time [Months]	ABC	GCB
60.000	62.532	71.429

SUPPLEMENTARY FIGURE S1. Overall survival (Kaplan-Meier) for ABC (N=54) and GCB subtype (N=77) as determined by IHC (immunohistochemical) determination; (p=0.27).

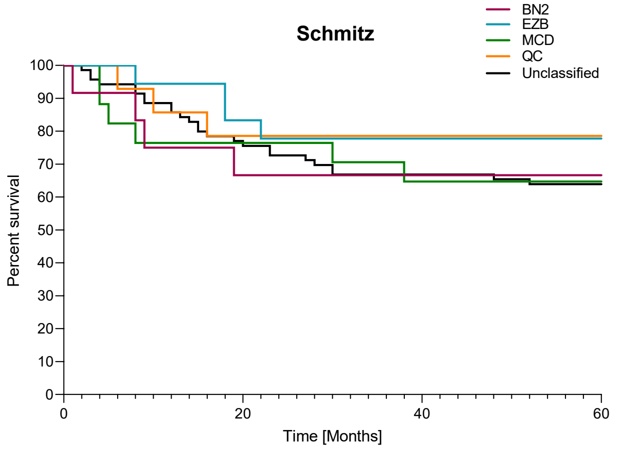
ABC = activated B-cell, GCB = germinal center B-cell



Time [Months]	ABC	GCB	QC	Unclassified
60.000	54.762	74.194	80.000	64.167

SUPPLEMENTARY FIGURE S2. Overall survival (Kaplan-Meier) according to the NGS classification; (p=0.06).

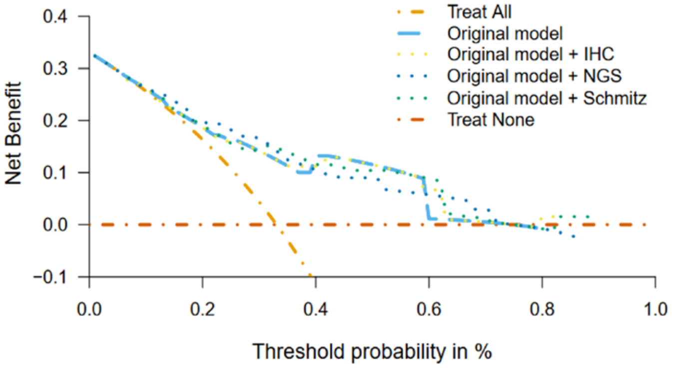
NGS = next generation sequencing, ABC = activated B-cell, GCB = germinal center B-cell, QC failed group = could not provide a clear result



Time [Months]	BN2	EZB	MCD	QC	Unclassified
60.000	66.667	77.778	64.706	78.571	63.941

SUPPLEMENTARY FIGURE S3. Overall survival (Kaplan-Meier) of new genetic subtypes determined by NGS according to the Schmitz's classification. (p=0.61).

NGS = next generation sequencing



SUPPLEMENTARY FIGURE S4. Net benefit at different threshold probabilities for different ways of deciding which patients require further treatment.

IHC = immunohistochemical classification, NGS = next generation sequencing classification

SUPPLEMENTARY TABLE S1. Cox proportional model: association between OS, IPI score and IHC determination of COO

	P value	HR	95% CI
COO by IHC	0.300		
IPI	**<0.001**	1.873	1.48 - 2.369
Lin	0.000		
Quad	0.722		
Cub	0.239		

COO = cell of origin, IHC = immunohistochemical determination, HR = hazard ratio, CI = confidence interval, Lin = linear function, Quad = quadratic function, Cub = cubic function

SUPPLEMENTARY TABLE S2. Cox proportional model: association between OS, IPI score and NGS determination of COO

	P value	HR	95% CI
COO by NGS	0.053		
IPI	**<0.001**	1.813	1.436 - 2.291
Lin	0.000		
Quad	0.616		
Cub	0.259		

COO = cell of origin, NGS = next generation sequencing, HR = hazard ratio, CI = confidence interval, Lin = linear function, Quad = quadratic function, Cub = cubic function

SUPPLEMENTARY TABLE S3. Cox proportional model: association between OS, IPI score and new genetic types classification by NGS

	P value	HR	95% CI
New genetic types by NGS	0.356		
IPI	**<0.001**	1.857	1.483 - 2.326
Lin	0.000		
Quad	0.784		
Cub	0.327		

NGS = next generation sequencing), HR = hazard ratio, CI = confidence interval, Lin = linear function, Quad = quadratic function, Cub = cubic function

SUPPLEMENTARY TABLE S4. Corrected internal discrimination 5 years after diagnosis

	Uno AUC
Internal	0.77
Internal + COO by IHC	0.77
Internal + COO by NGS	0.75
Internal + new genetic subtypes by NGS	0.75

COO = cell of origin, IHC = immunohistochemical determination, NGS = next generation sequencing, AUC = area under the curve

SUPPLEMENTARY TABLE S5. Calibration (values close to 1 represent good calibration and values close to 0.5 represent poor calibration)

	Mean t	Mean interval	Weak t	Weak interval
No classification				
Fixed internal	0.97	1.00	1.03	1.03
COO by IHC				
Fixed internal	0.97	0.99	0.91	0.92
COO by NGS				
Fixed internal	0.98	0.98	0.91	0.92
New genetic subtypes by NGS				
Fixed internal	0.98	0.97	0.87	0.88

COO = cell of origin, IHC = immunohistochemical determination, NGS = next generation sequencing

SUPPLEMENTARY TABLE S6. Brier score and IPA (Index of Prediction Accuracy)

	Brier	IPA
Corr. internal	0.18	0.20
Corr. internal + COO by IHC	0.18	0.19
Corr. internal + COO by NGS	0.18	0.18
Corr. internal + new genetic types by NGS	0.18	0.17

COO = cell of origin, IHC = immunohistochemical determination, NGS = next generation sequencing

SUPPLEMENTARY TABLE S7. Net benefit to patients when using different models to decide on additional treatment

Threshold	0.110	0.250	0.500	0.800
Net benefit - treat all	0.248	0.108	-0.338	-2.346
Net benefit - basic model with only IPI	0.254	0.167	0.115	-0.008
Net benefit - extended model with COO by IHC	0.254	0.167	0.115	-0.008
Net benefit - extended model with COO by NGS	0.255	0.182	0.085	-0.008
Net benefit - extended model with new genetic types by NGS	0.257	0.156	0.108	-0.008

COO = cell of origin, IHC = immunohistochemical determination, NGS = next generation sequencing