Supplemental data.

Supplemental Table 1. Patient characteristics for all individual trials.

		Total (n=323)	HOVON-130 (n=54)[23]	HOVON-84 (n=137)[24]	PETAL (n=132)[25]
Gender	Male	185 (57)	41 (76)	68 (49.6)	76 (58)
	Female	138 (43)	13 (24)	69 (50.4)	56 (42)
Age (IQR)		63 (53-71)	63 (54-72)	65 (55-72)	62 (53-69)
Ann Arbor Stage	1	23 (7)			23 (17)
	2	54 (17)	7 (13)	21 (15.3)	26 (20)
	3	73 (23)	6 (11)	40 (29.2)	27 (21)
	4	173 (54)	41 (76)	76 (55.5)	56 (42)
LDH	normal	124 (38)	14 (26)	50 (37)	60 (46)
	> normal	199 (62)	40 (74)	87 (64)	72 (55)
Extranodal involvement	0-1	204 (63)	27 (50)	81 (59)	96 (73)
	>1	119 (37)	27 (50)	56 (41)	36 (27)
WHO performance status	0	186 (58)	32 (59)	86 (63)	68 (52)
	1	100 (31)	18 (33)	36 (26)	46 (35)
	2	33 (10)	3 (6)	15 (11)	15 (11)
	3	4 (1)	1 (2)		3 (2)
IPI	Low	83 (26)	9 (17)	28 (20)	46 (35)
	Low-intermediate	65 (20)	9 (17)	31 (23)	25 (19)
	High-intermediate	104 (32)	25 (46)	42 (31)	37 (28)
	High	71 (22)	11 (20)	36 (26)	24 (18)
MYC	Negative	245 (76)		122 (89)	123 (93)
	MYC-SH	24 (7)	14 (26)	5 (4)	5 (4)
	Double/triple hit	54 (17)	40 (74)	10 (7)	4 (3)
Treatment	6x R-CHOP	99 (31)		46 (34)	53 (40)
	8x R-CHOP	29 (9)		25 (18)	4 (3)
	6x R-CHOP + 2xR	71 (22)			71 (54)
	6x RR-CHOP	44 (14)		44 (32)	
	8x RR-CHOP	22 (7)		22 (16)	
	Burkitt protocol	4 (1)			4 (3)
	6x R2-CHOP + 2xR	54 (17)	54 (100)		

Abbreviations: IQR: interquartile range, LDH: lactose dehydrogenase. WHO: world health organization, IPI: international prognostic index, MYC-SH: single hit *MYC* rearrangement, R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, RR-CHOP: R-CHOP with rituximab intensification, Burkitt protocol: 2x R-CHOP followed by a burkitt protocol consisting of high-dose methotrexate, cytarabine, hyperfractionated cyclophosphamide and ifosfamide, split-dose doxorubicin and etoposide, vincristine, vindestine and dexamethasone and R2-CHOP: R-CHOP combined with lenalidomide.

Supplemental Table 2. Descriptive statistics of radiomics features stratified for *MYC* rearrangement status

	MYC-wt DLBCL (n=245)		*MYC*-SH DLBCL (n=24)		Double/triple hit (n=54)	
	Median (IQR)	*Range*	*Median (IQR)*	*Range*	*Median (IQR)*	*Range*
SUV_{peak}	17.0 (11.8 - 22.4)	2.5 - 48.5	12.0 (8.7 - 16.7)	3.8 - 38.1	17.4 (12.9 - 23.4)	4.8 - 42.2
SUV_{max}	20.6 (15.2 - 28.3)	4.1 - 75.1	14.9 (10.5 - 20.6)	4.3 - 44.5	20.6 (15.9 - 27.8)	5.8 - 46.8
SUV_{mean}	8.3 (6.5 - 10.0)	4.1 - 19.3	6.9 (5.4 - 8.2)	4.3 - 15.9	8.6 (6.8 - 10.2)	4.3 - 15.9
TLG	2288.5 (561.2 - 6207.2)	0.3 - 36586.4	2141.2 (92.5 - 8950.3)	1.4 - 34264.8	6383.3 (2004.0 - 11870.8)	61.1 - 47965.7
MTV	256.6 (54.9 - 777.0)	0.1 - 4746.7	292.5 (15.9 - 1098.7)	0.3 - 4467.0	709.5 (304.6 - 1280.1)	13.5 - 5598.5
Number of lesions	7 (3 - 16)	1 - 103	5 (1 - 15)	1 - 69	10 (3.3 - 23.5)	1 - 161
$Dmax_{bulk}$	28.2 (8.8 - 43.6)	0 - 74.3	28.6 (0 - 50.2)	0 - 99.5	35.3 (23.0 - 51.5)	0 - 97.1
$Spread_{bulk}$	1011.5 (138.3 - 3086.8)	0 - 47578.5	767.5 (0 - 4047.9)	0 - 17103.4	1978.0 (575.4 - 7674.8)	0 - 43732.3
$Dmax_{patient}$	37.3 (9.0 - 58.4)	0 - 86.1	42.3 (0 - 62.5)	0 - 131.2	50.4 (32.4 - 76.1)	0 - 110.3
$Spread_{patient}$	3122.0 (156.7 - 25383.9)	0 - 1514730	2099.7 (0 - 18197.4)	0 - 678819	11828.1 (1034.3 - 77878.9)	0 - 3263620
$VolumeSpread_{bulk}$	923.0 (18.9 - 4943.2)	0 - 202877	275.8 (0 - 10912.3)	0 - 227263.0	2623.0 (426.5 - 17188.3)	0 - 164012.0
$Volumemax_{patient}$	114.5 (11.0 - 497.0)	0 – 4651.1	118.2 (0 - 700.7)	0 - 3556.5	444.7 (88.3 - 752.8)	0 - 5397.8
$VolumeSpread_{patient}$	1138.9 (23.4 - 7260.1)	0 - 213659	309.1 (0 - 10985.2)	0 - 251000.0	4586.2 (462.5 - 32641.3)	0 - 314464
$DSUVpeak_{bulk}$	10.2 (2.0 - 15.8)	0 - 44.4	5.0 (0 - 10.3)	0 - 33.7	10.8 (5.6 - 17.5)	0 - 37.8
$DSUVpeaksum_{bulk}$	57.8 (5.8 - 154.1)	0 - 1901.6	21.8 (0 - 84.6)	0 - 1042.9	80.3 (19.6 - 261.8)	0 - 1360.2
$DSUVpeak_{patient}$	10.5 (2.2 - 16.7)	0 - 44.4	5.0 (0 - 10.3)	0 - 33.7	10.8 (5.6 - 19.2)	0 - 37.8
$DSUVpeaksum_{patient}$	104.7 (8.7 - 483.8)	0 - 16300.6	52.6 (0 - 119.5)	0 - 9410.3	226.5 (27.5 - 1195.0)	0 - 15053.4
$DSUVpeaksum_{hottest}$	59.2(6.8 - 167.6)	0 - 1974.4	21.8 (0 - 84.6)	0 - 1729.1	80.3 (21.1 - 261.8)	0 - 1360.2

Supplemental Table 3. H-statistics and p values of radiomics features per *MYC* group

	All groups		*MYC*-wt *vs MYC*-SH		*MYC*-wt vs double/triple hit		*MYC*-SH vs double/triple hit	
	H-statistic	p value	H-statistic	p value	H-statistic	p value	H-statistic	p value
SUV_{peak}	5.67	0.06	-	-	-	-	-	-
SUV_{max}	6.27	0.04	-2.47	0.04	0.10	0.92	2.21	0.04
SUV_{mean}	7.26	0.03	-2.53	0.02	0.59	0.56	2.57	0.02
TLG	13.80	<0.01	-0.21	0.84	3.65	<0.01	2.42	0.02
MTV	13.72	<0.01	0.00	1.00	3.67	<0.01	2.26	0.04
Number of lesions	5.86	0.05	-0.89	0.37	2.12	0.06	2.07	0.06
$Dmax_{bulk}$	7.17	0.03	0.07	0.95	2.66	0.02	1.58	0.17
$Spread_{bulk}$	7.52	0.02	-0.47	0.64	2.62	0.03	2.02	0.07
$Dmax_{patient}$	11.55	<0.01	0.10	0.92	3.38	<0.01	1.99	0.07
$Spread_{patient}$	7.17	0.03	-0.65	0.52	2.49	0.04	2.09	0.05
$VolumeSpread_{bulk}$	11.31	<0.01	-0.21	0.84	3.30	<0.01	2.20	0.04
$Volumemax_{patient}$	12.02	<0.01	0.07	0.94	3.45	<0.01	2.05	0.06
$VolumeSpread_{patient}$	11.52	<0.01	-0.31	0.76	3.31	<0.01	2.30	0.03
$DSUVpeak_{bulk}$	5.79	0.06	-	-	-	-	-	-
$DSUVpeaksum_{bulk}$	6.87	0.03	-1.34	0.18	2.06	0.06	2.43	0.04
$DSUVpeak_{patient}$	5.93	0.05	-1.83	0.10	1.36	0.17	2.43	0.05
$DSUVpeaksum_{patient}$	7.11	0.03	-1.47	0.14	2.02	0.07	2.52	0.04
$DSUVpeaksum_{hottest}$	6.78	0.03	-1.40	0.16	2.00	0.07	2.45	0.04

Supplemental Table 4. Relative feature importance of individual predictors in multivariate logistic regression models

	IPI + MYC	IPI + MYC + MTV	Radiomics	Radiomics + MYC
Estimate	-3.355	-3.063	-1.733	-2.033
IPI 2	1.379	1.143		
3	2.018	1.538		
4	2.050	1.465		
MYC MYC-SH	1.261	1.309		0.895
Double/triple hit	1.344	1.225		1.209
MTV		0.500	1.003	0.925
$Dmax_{bulk}$			0.756	0.698
$DSUVpeak_{patient}$			-0.631	-0.592
$Spread_{patient}$			-0.266	-0.309

Abbreviations: IPI: international prognostic index, MYC-SH: single hit MYC rearrangement, MTV: metabolic tumor volume

Supplemental Table 5. Concordance and disconcordance between high-risk and low-risk patients as identified by the IPI risk score, MYC rearrangement status and the radiomics+MYC prediction model.

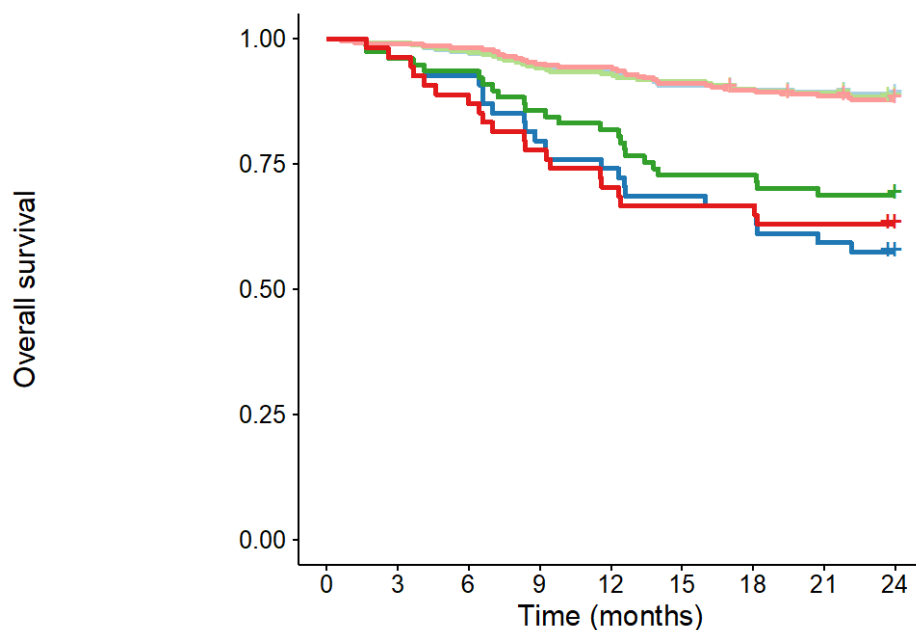|	IPI high	IPI low	MYC high	MYC low	Rad+myc high	Rad+myc low
IPI high	71	0	16	55	25	46
IPI low	0	252	38	214	41	211
MYC high	16	38	54	0	35	19
MYC low	214	55	0	269	31	238
Rad+myc High	25	41	35	31	66	0
Rad+myc low	46	211	19	238	0	257

Abbreviations: IPI: international prognostic index, Rad+myc: radiomics+MYC prediction model.

Supplemental Table 6. Survival rates of high risk and low risk patients according to prediction models using 2-year progression free survival (PFS) and 2-year overall survival (OS) as outcome parameter

		PFS (95% CI)	OS (95% CI)
IPI	low	92.9 (87.7-98.5)	94.1 (89.2-99.3)
	low-intermediate	80.6 (71.7-90.6)	89.6 (82.5-97.2)
	high-intermediate	69.8 (61.6-79.1)	83.0 (76.1-90.5)
	high	64.9 (55.1-76.5)	68.8 (59.2-80.0)
MYC	*MYC*-wt	81.7 (77.1-86.6)	87.9 (84.0-92.0)
	MYC-SH	66.7 (50.2-88.5)	82.9 (69.0-99.7)
	Double/triple hit	57.4 (45.6-72.2)	64.8 (53.3-78.9)
IPI *MYC*	low	83.5 (78.9-88.4)	89.8 (86.1-93.8)
	high	60.6 (51.7-71.0)	69.6 (61.1-79.3)
IPI *MYC* MTV	low	82.9 (78.4-87.6)	88.6 (85.0-92.4)
	high	56.4 (46.4-68.6)	59.3 (47.5-73.9)
Radiomics	low	84.0 (79.7-88.6)	87.9 (84.1-91.8)
	high	52.6 (42.6-64.9)	63.0 (51.3-77.3)
Radiomics + *MYC*	low	84.8 (80.5-89.3)	89.0 (85.4-92.7)
	high	50.6 (40.7-63.0)	57.4 (45.6-72.2)

Abbreviations: CI: confidence interval, IPI: international prognostic index, MYC-wt: MYC wild type, MYC-SH: single hit MYC rearrangement, MTV: metabolic tumor volume.

Supplemental Figure 1. Kaplan-Meier survival curves of high-risk and low-risk groups for 2-year overall survival

Number at risk

low Radiomics+MYC	281	278	273	266	263	255	251	249	247
high Radiomics+MYC	54	52	50	43	40	37	36	32	30
low IPI	258	256	251	243	240	236	231	228	224
high IPI	77	74	72	66	63	56	56	53	53
low Radiomics	281	278	276	267	265	256	251	247	244
high Radiomics	54	52	47	42	38	36	36	34	33