Figures

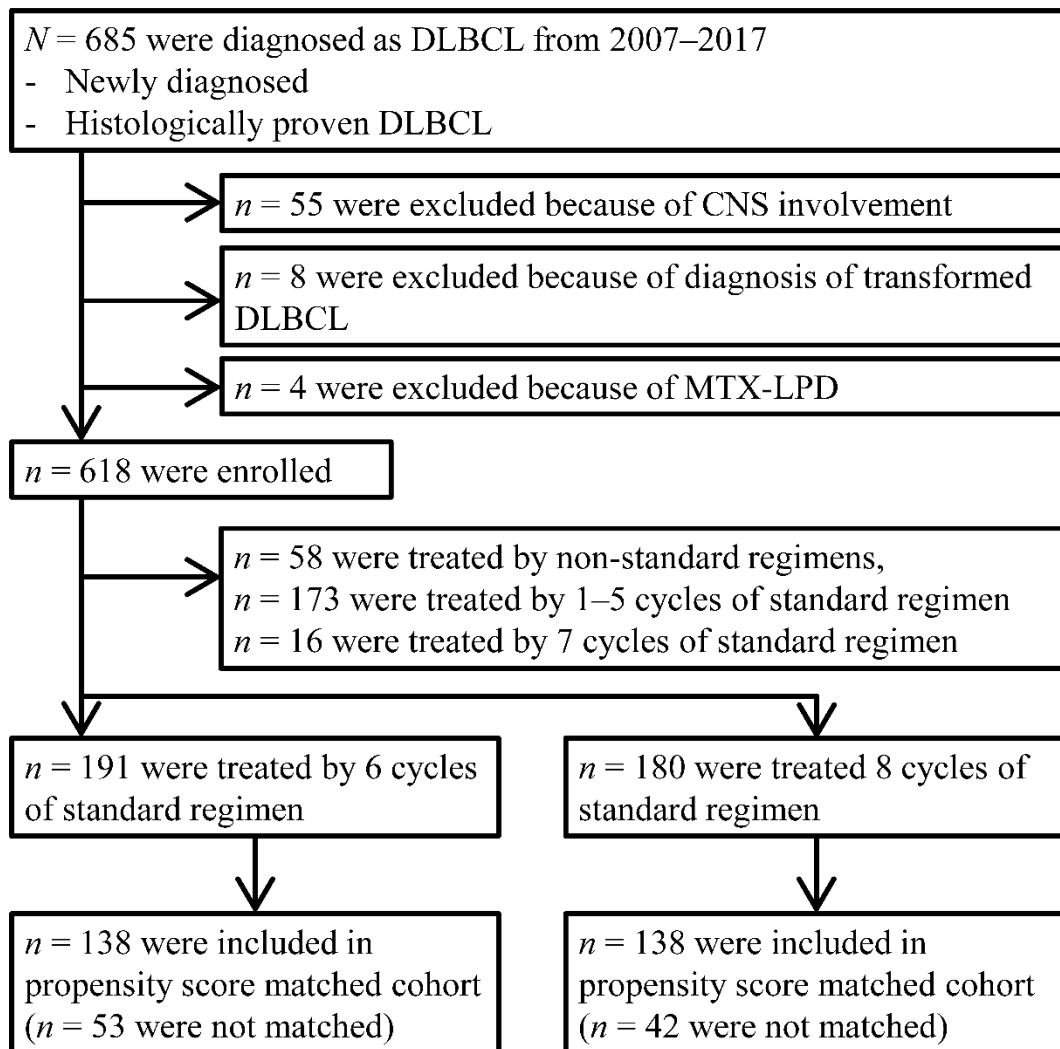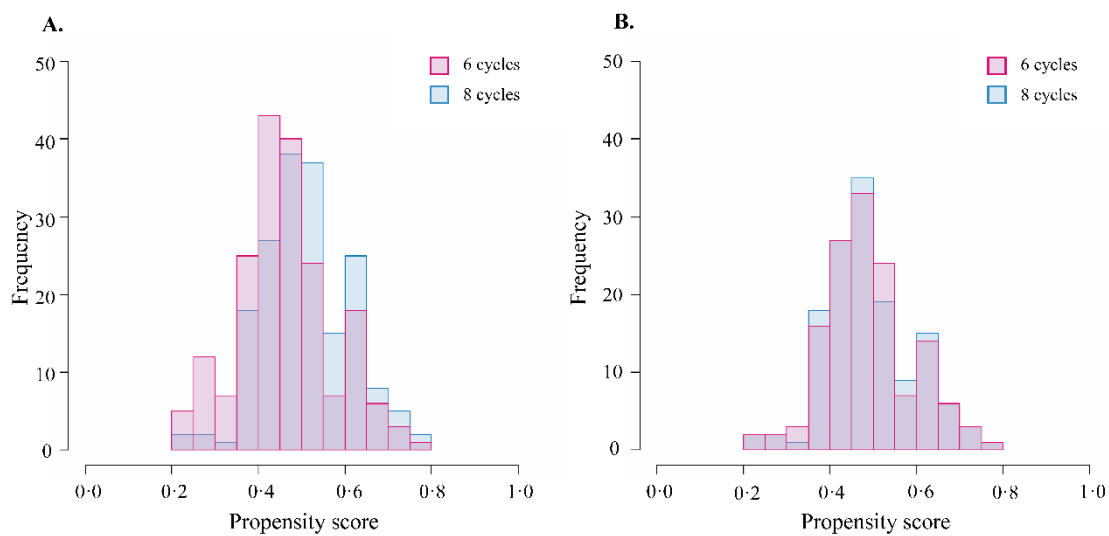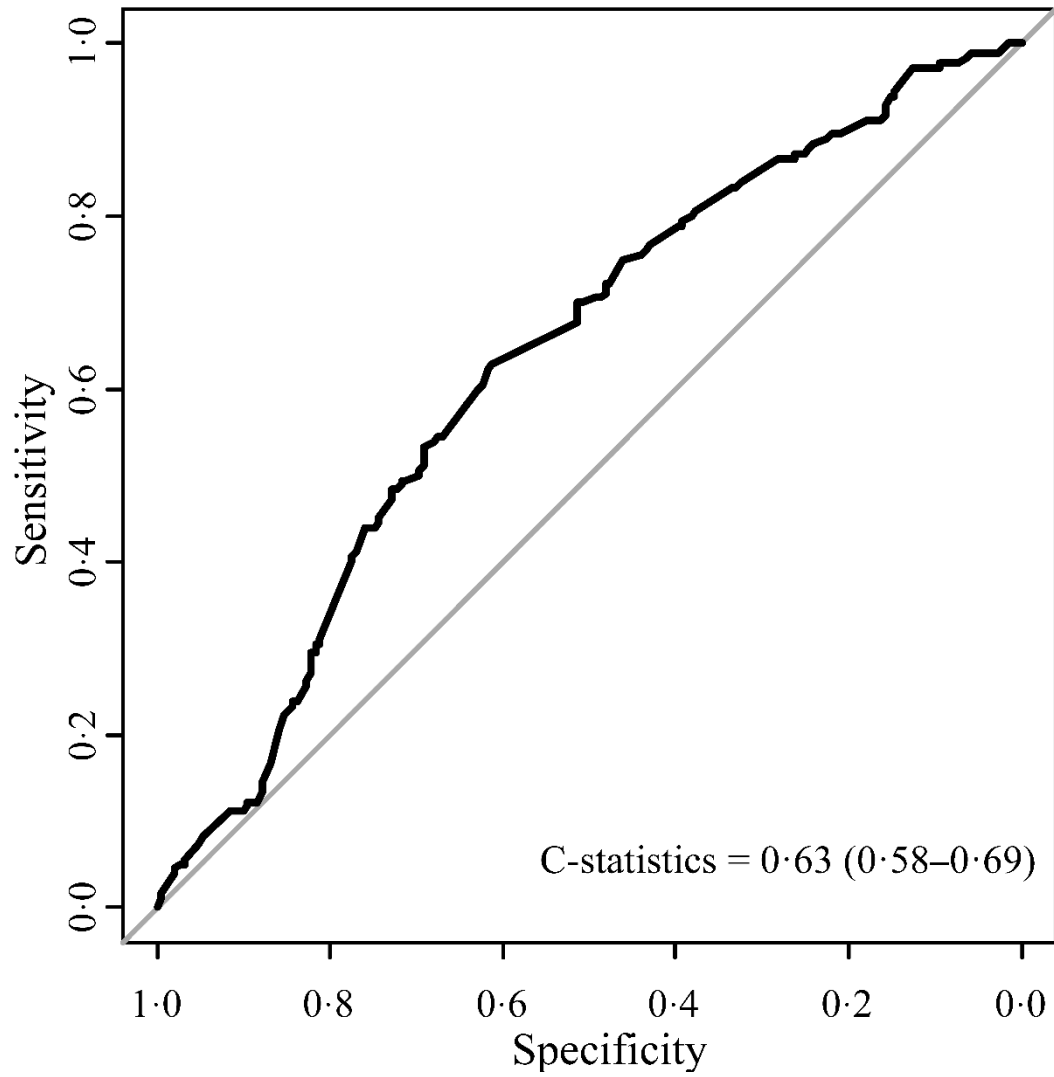**Online Supplementary Figure S1. Flowchart for patient selection.**

CNS = central nervous system; DLBCL = diffuse large B-cell lymphoma; MTX-LPD = methotrexate-associated lymphoproliferative disorder.

Online Supplementary Figure S2. Histograms of propensity scores.
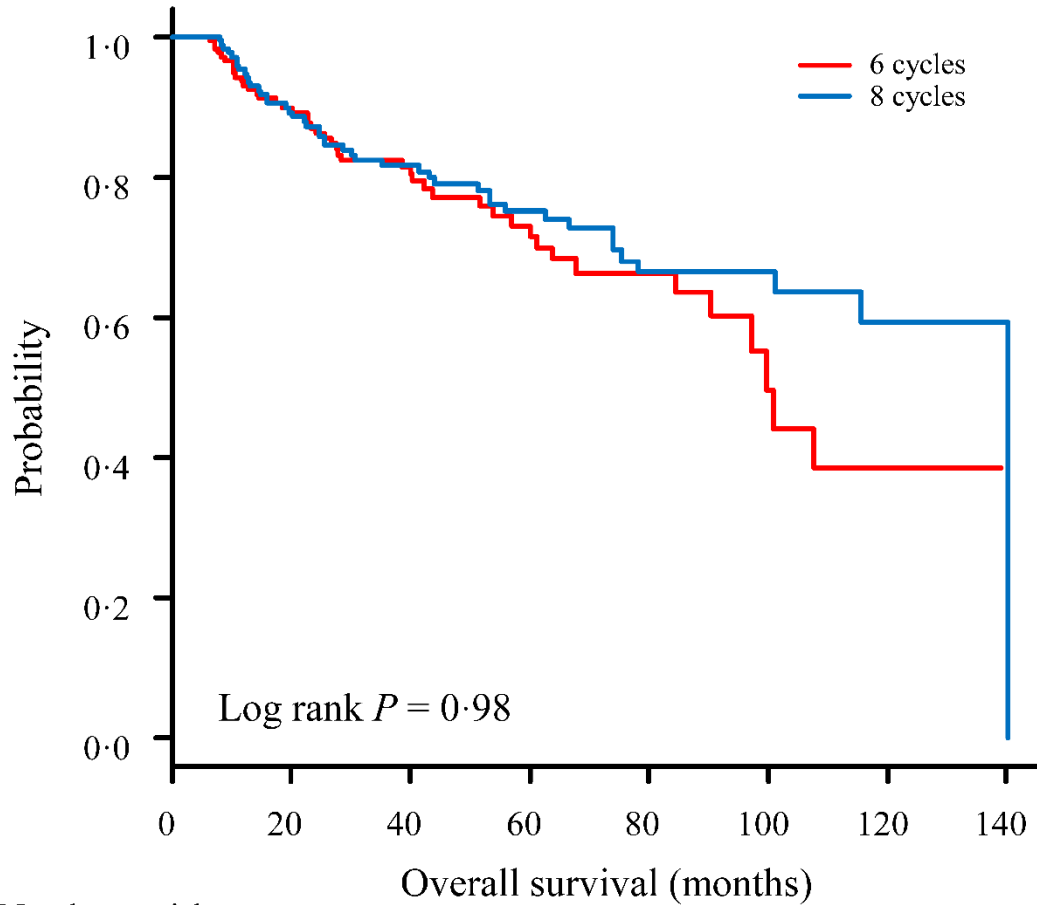

A) Original data set. **B)** Matched data set.

Online Supplementary Figure S3. Receiver operating characteristic curves showing c-statistics for propensity scores.

C-statistics = 0·63 (0·58–0·69)
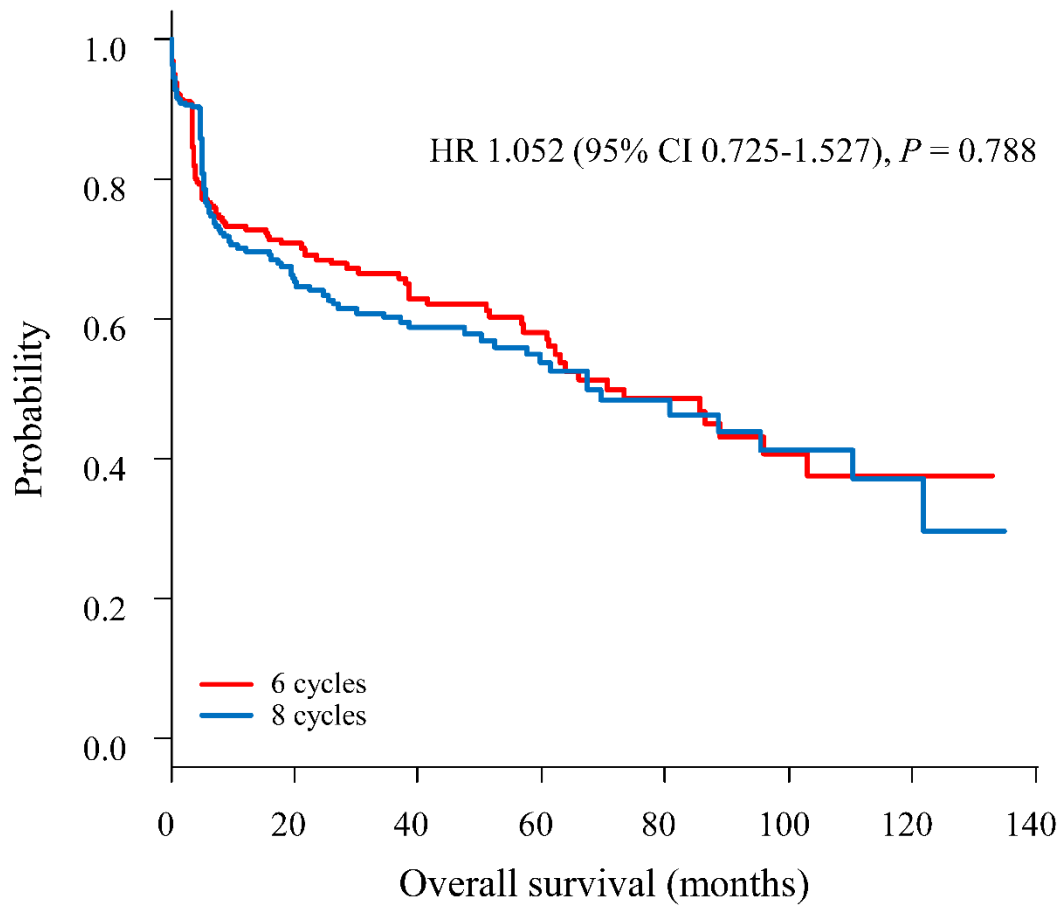
Online Supplementary Figure S4. Kaplan-Meier survival curve of overall survival using the original data set according to the number of cycles of regimens.

Online Supplementary Figure S5. Time-varying Kaplan-Meier survival curve of overall survival using the matched data set according to the number of cycles of regimens.

HR 1.052 (95% CI 0.725-1.527), $P = 0.788$

6 cycles
8 cycles

Online Supplementary Figure S6. Covariate-adjusted Cox hazards model with restricted cubic spline with three knots showing the association between tARDI and overall survival according to the number of cycles of regimens using the original data set.
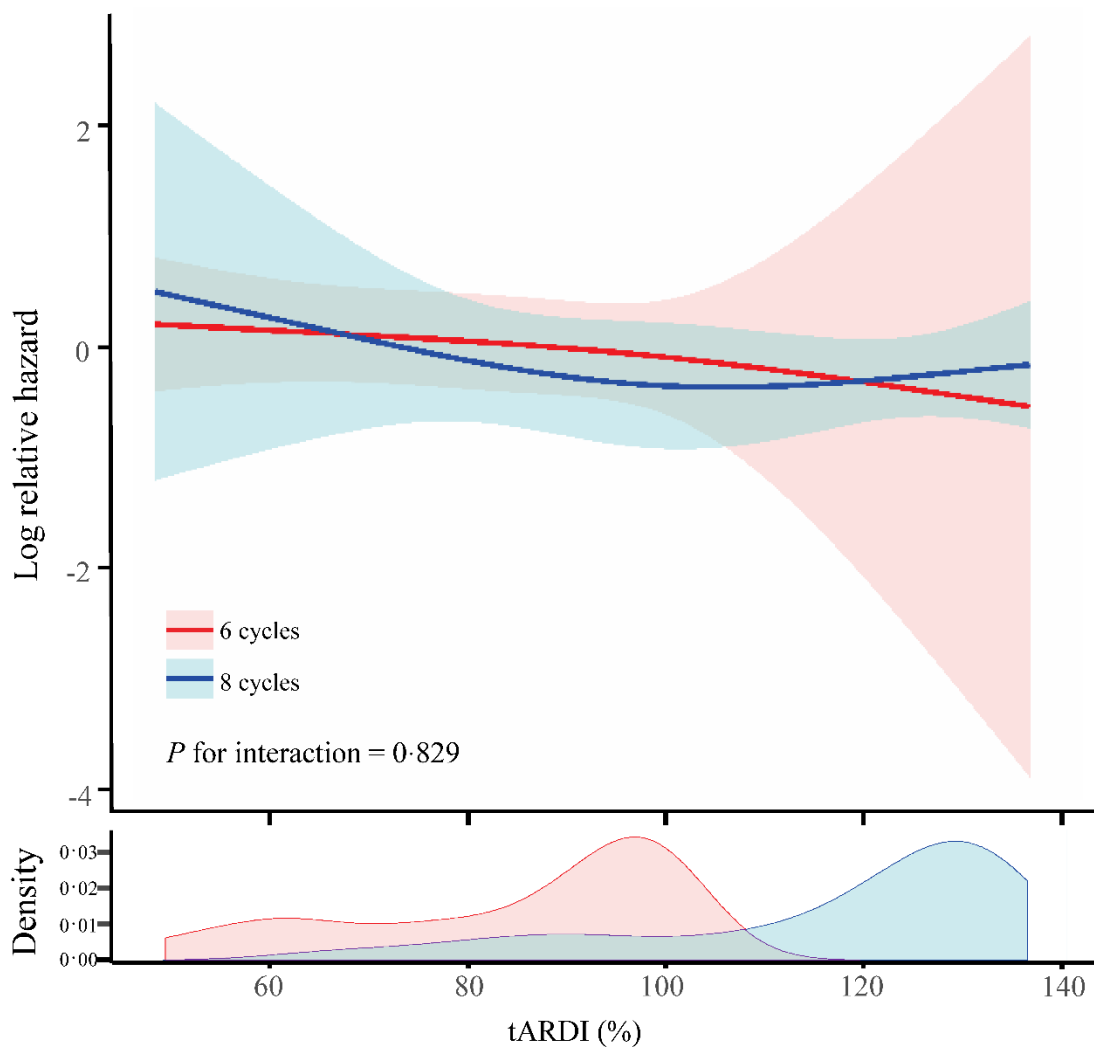
Solid line represents log hazard ratio. Shaded area is the 95% confidence interval.

tARDI = total average relative dose intensity.

Online Supplementary Figure S7. Covariate-adjusted Cox hazards model with restricted cubic spline with three knots showing the association between age and overall survival according to the number of cycles of regimens using the original data set.

Solid line represents the log hazard ratio. Shaded area is the 95% confidence interval.

Online Supplementary Figure S8. Covariate-adjusted Cox hazards model with restricted cubic spline with three knots showing associations between tARDI and overall survival of six groups divided by each score of the IPI using the matched data set.

Solid line represents the log hazard ratio. Shaded area is the 95% confidence interval.

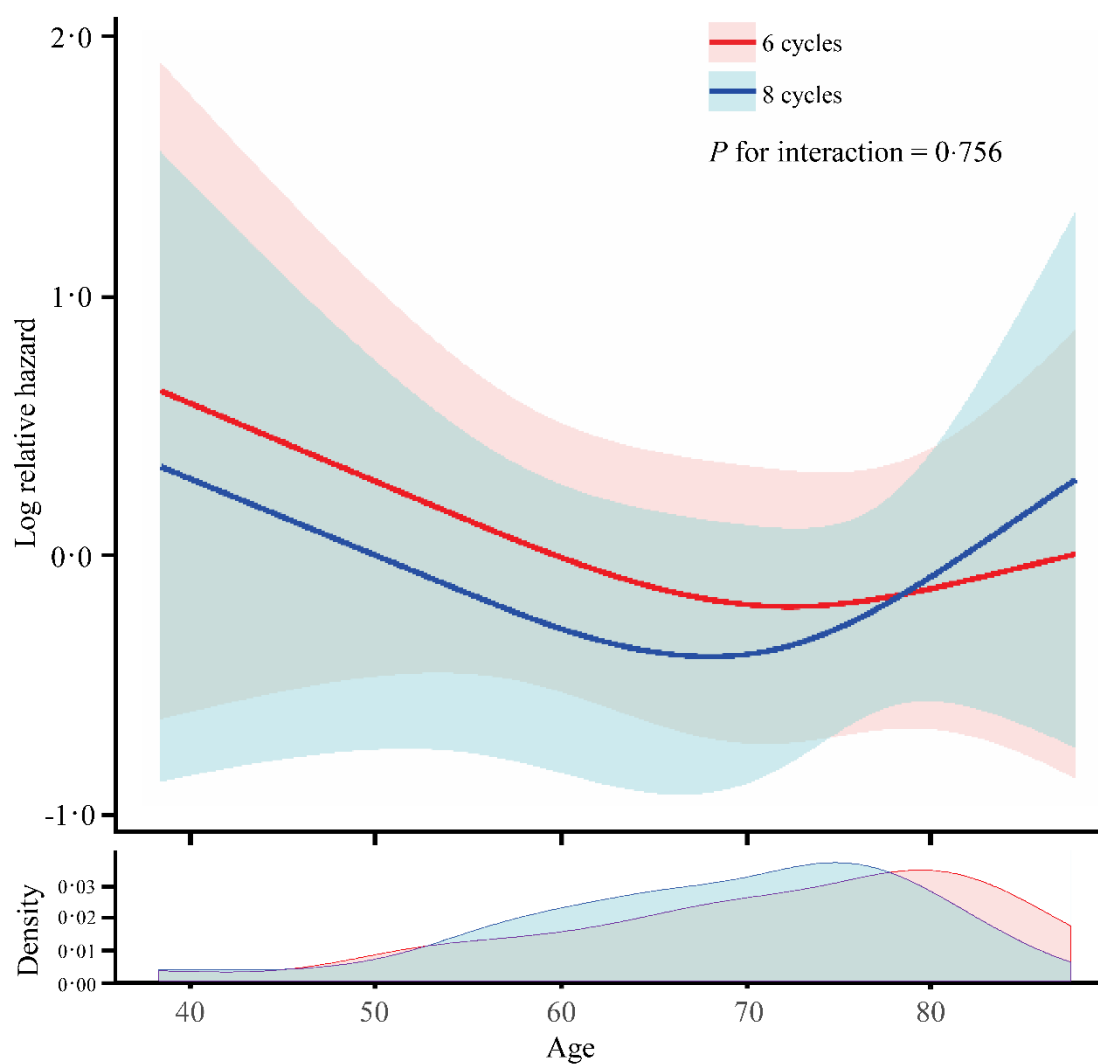IPI = International Prognostic Index; tARDI = total average relative dose intensity.

Online Supplementary Figure S9. Covariate-adjusted Cox hazards model with restricted cubic spline with three knots showing associations between tARDI and overall survival of six groups divided by each score of the IPI using the original data set.
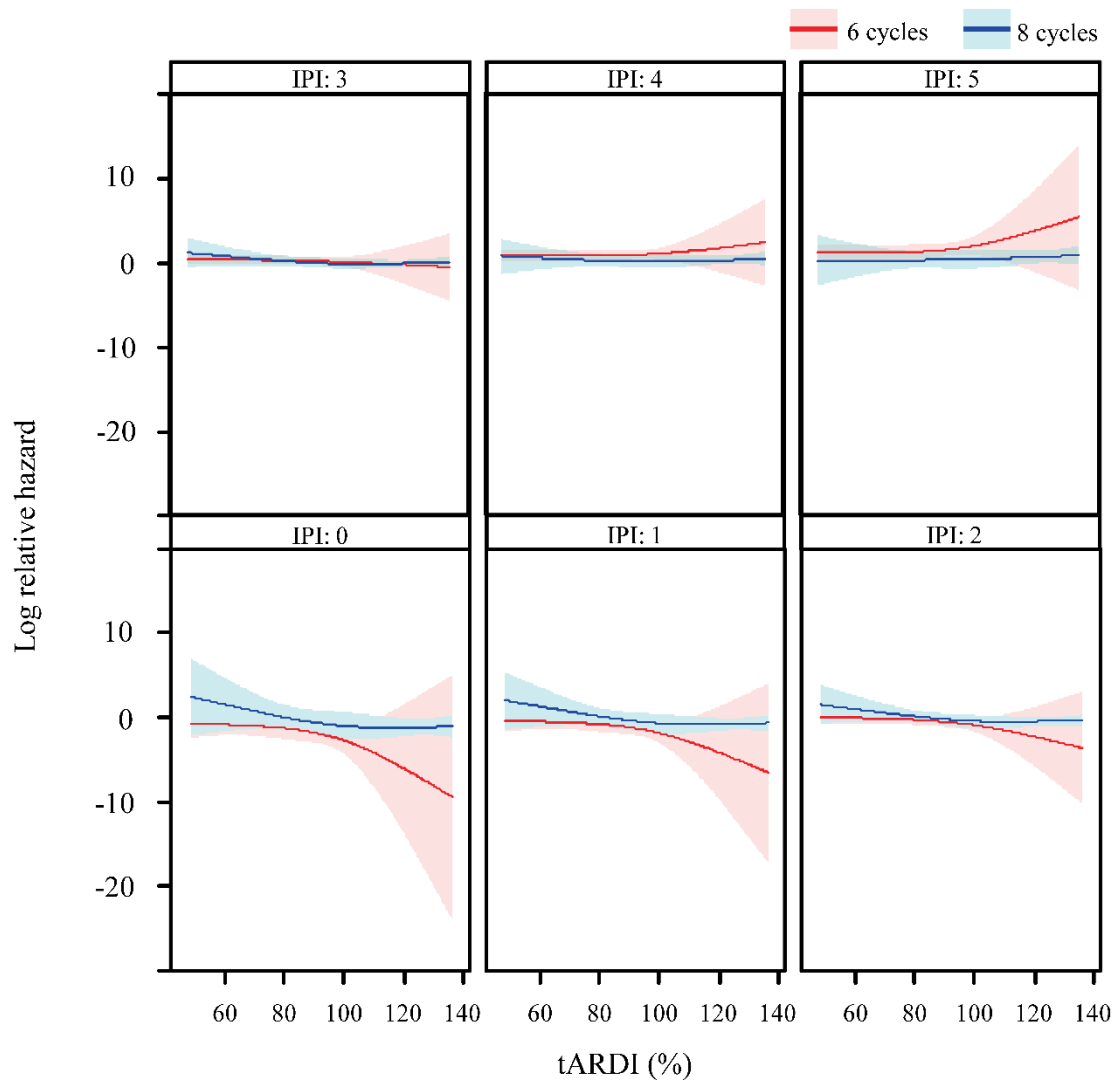
Solid line represents the log hazard ratio. Shaded area is the 95% confidence interval.

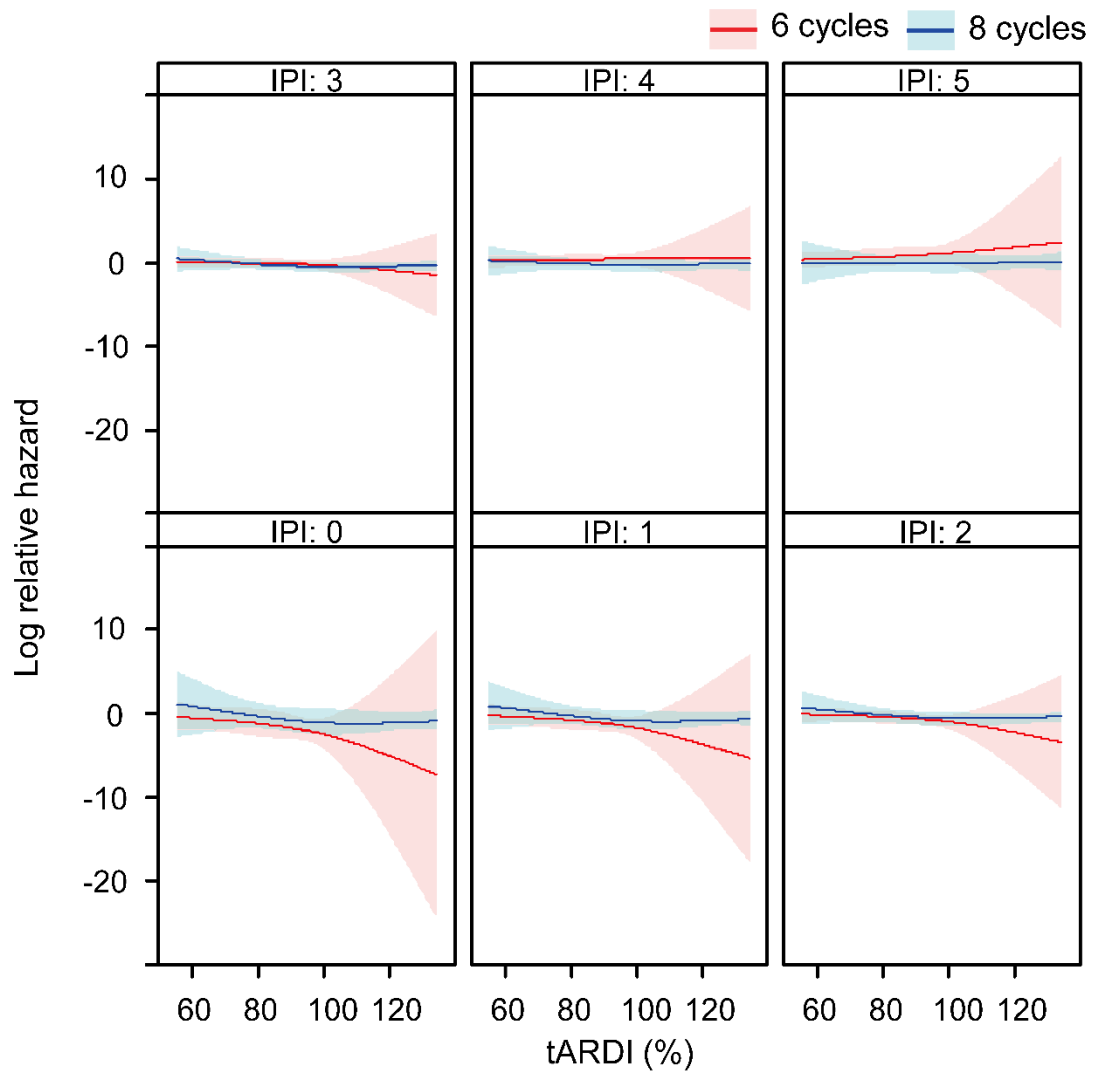IPI = International Prognostic Index; tARDI = total average relative dose intensity.

Online Supplementary Figure S10. Covariate-adjusted Cox hazards model with restricted cubic spline with three knots showing associations between tARDI and overall survival for binary groups divided by IPI (<3 versus ≥3).
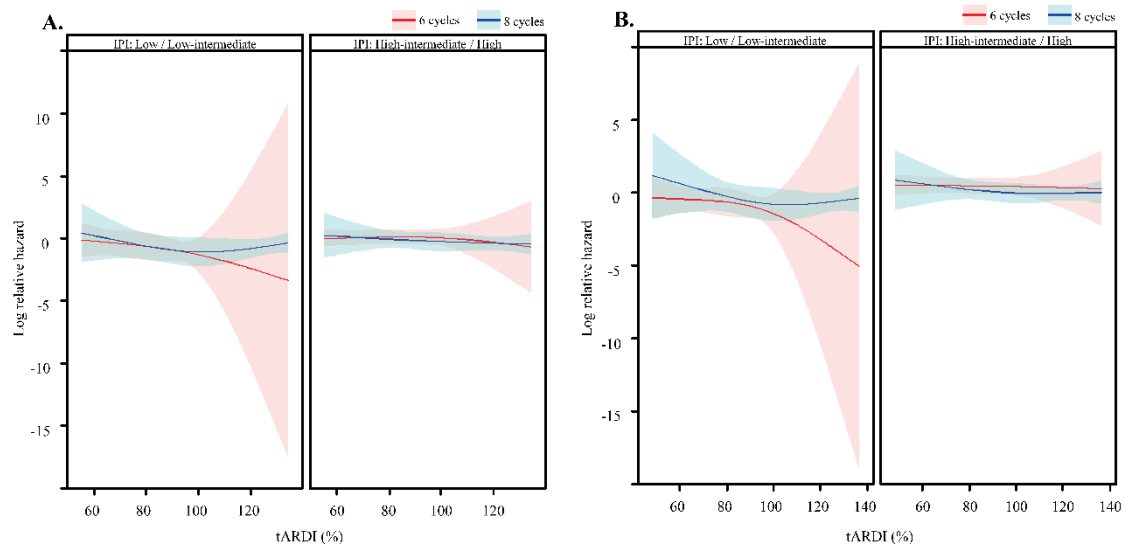
Solid line represents log hazard ratio. Shaded area is the 95% confidence interval. **A)** Matched data set. **B)** Original data set. IPI = International Prognostic Index; tARDI = total average relative dose intensity.

Online supplementary table 1. Patient characteristics at diagnosis before propensity score matching.

	All patients		Six cycles of standard regimens		Eight cycles of standard regimens		*P* value	Survivor		Non-survivor		*P* value
	(*N* = 371)		(*n* = 191)		(*n* = 180)			(*n* = 281)		(*n* = 90)		
Age, y - median, range	71	(27–90)	73	(27–90)	69	(22–87)	0.003	71	(27–90)	72	(33–89)	0.079
≥70	201	(54.2)	113	(59.2)	88	(48.9)	0.049	148	(52.7)	53	(58.9)	0.332
Male - n (%)	193	(52.0)	105	(55.0)	88	(48.9)	0.254	143	(50.9)	50	(55.6)	0.469
ECOG PS ≥2 - n (%)	75	(20.2)	43	(22.5)	32	(17.8)	0.301	40	(14.2)	35	(38.9)	<0.001
Extranodal sites ≥2 - n (%)	123	(33.2)	59	(30.9)	64	(35.6)	0.378	87	(31.0)	36	(40.0)	0.124
Ann Arbor stage III/IV - n (%)	235	(63.3)	112	(58.6)	123	(68.3)	0.067	165	(58.7)	70	(77.8)	0.001
Elevated LDH (>ULN) - n (%)	236	(63.6)	111	(58.1)	125	(69.4)	0.024	165	(58.7)	71	(78.9)	<0.001
Serum albumin (g/dl) - median, range	3.6	(1.1–5.1)	3.5	(1.4–5.1)	3.7	(1.1–5.1)	0.191	3.7	(1.1–5.1)	3.4	(1.6–4.9)	0.001
IPI - n (%)												
Low / Low intermediate (0-2)	173	(46.6)	94	(49.2)	79	(43.9)	0.349	149	(53.0)	24	(26.7)	<0.001
High intermediate / High (≥3)	198	(53.4)	97	(50.8)	101	(56.1)		132	(47.0)	66	(73.3)	
NCCN-IPI - n (%)												
Low / Low intermediate (0-3)	137	(36.9)	71	(37.2)	66	(36.7)	0.999	121	(43.1)	16	(17.8)	<0.001
High intermediate / High (≥4)	234	(63.1)	120	(62.8)	114	(63.3)		160	(56.9)	74	(82.2)	
Bulky mass - n (%)	77	(20.8)	40	(20.9)	37	(20.6)	0.999	51	(18.1)	26	(28.9)	0.036
B symptoms - n (%)	119	(32.1)	61	(31.9)	58	(32.2)	0.999	81	(28.8)	38	(42.2)	0.020
Uric acid (mg/dl) - median, range	5.1	(0.2–23.0)	5.3	(0.2–14.3)	5.0	(1.1–23.0)	0.169	5.0	(0.2–23.0)	5.9	(0.7–13.7)	0.036
≥7.5 mg/dL	45	(12.1)	23	(12.0)	22	(12.2)	0.999	29	(10.3)	16	(17.8)	0.065
sIL-2R - median, range	1,300	(125–38,400)	1,200	(168–38,400)	1,478	(125–25,400)	0.271	1,120	(125–31,000)	2,740	(316–38,400)	<0.001
≥median	185	(49.9)	86	(45.0)	99	(55.0)	0.062	127	(45.2)	58	(64.4)	0.002
CCI - n (%)												
Low / Medium (0-2)	321	(86.5)	163	(85.3)	158	(87.8)	0.544	247	(87.9)	74	(82.2)	0.213
High / Very high (≥3)	50	(13.5)	28	(14.7)	22	(12.2)		34	(12.1)	16	(17.8)	
GNRI - n (%)												
No-risk group (>98)	139	(37.5)	80	(41.9)	59	(32.8)	0.086	91	(32.4)	48	(53.3)	<0.001
Risk group (≤98)	232	(62.5)	111	(58.1)	121	(67.2)		190	(67.6)	42	(46.7)	
Total ARDI	99.0	(19.2–142.6)	903	(19.2–106.4)	123.7	(61.2–142.6)	<0.001	99.6	(35.4–142.6)	92.2	(19.2–138.0)	0.010
ASCT	21	(5.7)	15	(7.9)	6	(3.3)	0.073	11	(3.9)	10	(11.1)	0.017
Up-front ASCT	13	(3.5)	13	(6.8)	0	(0.0)	<0.001	7	(2.5)	6	(6.7)	0.092
ASCT as salvage therapy	8	(2.2)	2	(1.0)	6	(3.3)	0.164	4	(1.4)	4	(4.4)	0.101

ASCT = autologous stem cell transplantation; CCI = Charlson Comorbidity Index; ECOG PS = Eastern Cooperative Oncology Group performance status; fTRST = Flemish

version of the Triage Risk Screening Tool; GNRI = Geriatric Nutritional Risk Index; IPI = International Prognostic Index; LDH = lactate dehydrogenase; NCCN = National Comprehensive Cancer Network; sIL-2R = soluble interleukin-2 receptor; SMD = standardized mean difference; ULN = upper limit of normal.

Online supplementary table 2. Patient characteristics between included and excluded patients.

	Standard regimens (N = 560)		Standard regimens with 1-5, 7 cycles (n = 189)		Standard regimens with 6, 8 cycles (n = 371)		P value
Age, y - median, range	73	(23–96)	76	(23–96)	71	(27–90)	<0.001
≥70	329	(58.8)	128	(67.7)	201	(54.1)	0.002
Male - n (%)	294	(52.5)	101	(53.4)	193	(52.0)	0.789
ECOG PS ≥2 - n (%)	157	(28.0)	82	(43.4)	75	(20.2)	<0.001
Extranodal sites ≥2 - n (%)	189	(33.8)	66	(34.9)	123	(33.2)	0.706
Ann Arbor Stage III/IV - n (%)	355	(63.4)	120	(63.54	235	(63.3)	0.999
Elevated LDH (>ULN) - n (%)	356	(63.6)	120	(63.5)	236	(63.6)	0.999
Serum albumin (g/dl) - median, range	3.5	(0.6–5.1)	3.3	(0.6–4.9)	3.6	(1.1–5.1)	0.001
IPI - n (%)							
Low / Low intermediate (0-2)	249	(44.5)	76	(40.2)	173	(46.6)	0.152
High intermediate / High (≥3)	311	(55.5)	113	(59.8)	198	(53.4)	
NCCN-IPI – n (%)							
Low / Low intermediate (0-3)	191	(34.1)	54	(28.6)	137	(36.9)	0.059
High intermediate / High (≥4)	369	(65.9)	135	(71.4)	234	(63.1)	
Bulky mass - n (%)	114	(20.4)	37	(19.6)	77	(20.8)	0.741
B symptoms - n (%)	188	(33.6)	69	(36.5)	119	(32.1)	0.254
Uric acid (mg/dl) - median, range	5.2	(0.2–23.0)	5.0	(0.3–15.6)	5.3	(0.2–23.0)	0.558
≥7.5 mg/dL	77	(13.8)	30	(15.9)	47	(12.7)	0.302
sIL-2R - median, range	1,415	(104–61,900)	1,466	(104–61,900)	1,336	(125–38,400)	0.668
≥median	269	(48.0)	95	(50.3)	174	(46.9)	0.475
CCI - n (%)							
Low / Medium (0-2)	237	(42.3)	58	(30.7)	179	(48.2)	<0.001
High / Very high (≥3)	323	(57.7)	131	(69.3)	192	(51.8)	
GNRI - n (%)							
No-risk group (>98)	217	(38.8)	60	(31.7)	157	(42.3)	0.013
Risk group (≤98)	343	(61.2)	129	(68.3)	214	(57.7)	
ASCT	25	(4.5)	4	(2.1)	21	(5.7)	0.081
Up-front ASCT	14	(2.5)	1	(0.5)	13	(3.5)	0.042
ASCT as salvage therapy	11	(2.0)	3	(1.6)	8	(2.2)	0.999

ASCT = autologous stem cell transplantation; CCI = Charlson Comorbidity Index; ECOG PS = Eastern Cooperative Oncology Group performance status; fTRST = Flemish

version of the Triage Risk Screening Tool; GNRI = Geriatric Nutritional Risk Index; IPI = International Prognostic Index; LDH = lactate dehydrogenase; NCCN = National Comprehensive Cancer Network; sIL-2R = soluble interleukin-2 receptor; ULN = upper limit of normal.

Online supplementary table 3. Time-varying Cox regression analysis of clinical factors significantly associated with overall survival.

	HR (95%CI)	*P* value
Male	1.227 (0.815-1.791)	0.289
IPI, score	1.257 (1.067-1.480)	0.006
Bulky mass	1.290 (0.856-1.943)	0.224
CCI, score	1.092 (0.970-1.229)	0.147
GNRI, score	0.989 (0.975-1.003)	0.133
Total ARDI, %	0.992 (0.983-1.001)	0.075
Eight cycles of standard regimens	1.538 (0.947-2.498)	0.082

ARDI = average relative dose intensity; CCI = Charlson Comorbidity Index; CI = confidence intervals; GNRI = Geriatric Nutritional Risk Index; HR = hazard ratio; IPI = International Prognostic Index.

Online supplementary table 4. Occurrence of non-hematological toxicity or febrile neutropenia ≥grade 3.

	All patients		Six cycles of standard regimens		Eight cycles of standard regimens		*P* value
	Original data						
Adverse event (Grade ≥3), n (%)	(*N* = 371)		(*n* = 191)		(*n* = 180)		
Febrile neutropenia	157	(42.3)	74	(38.7)	83	(46.1)	0.172
Non-hematological toxicity	117	(31.5)	59	(30.9)	58	(32.2)	0.823
	Matched data						
Adverse event (Grade ≥3), n (%)	(*N* = 276)		(*n* = 138)		(*n* = 138)		
Febrile neutropenia	125	(45.3)	56	(40.6)	69	(50.0)	0.147
Non-hematological toxicity	93	(33.7)	48	(34.8)	45	(32.6)	0.799

Online supplementary table 5. Multivariate logistic regression analysis for clinical factors associated with the occurrence of severe adverse events ≥grade 3.

	OR (95% CI)	*P* value
Male	0.828 (0.531–1.290)	0.407
IPI, score	1.250 (1.040–1.500)	0.017
Serum albumin, g/dL	0.721 (0.508–1.020)	0.068
Bulky mass	2.170 (1.190–3.950)	0.011
Total ARDI, %	1.010 (0.995–1.020)	0.218
CCI score, /point	1.180 (0.995–1.400)	0.058
Eight cycles of standard regimens	0.885 (0.483–1.620)	0.694

ARDI = average relative dose intensity; CCI = Charlson Comorbidity Index; CI = confidence intervals; G8 = Geriatric 8; IPI = International Prognostic Index; OR = odds ratio.