

Treatment Cost and Life Expectancy of Diffuse Large B-Cell Lymphoma (DLBCL)

A Discrete Event Simulation Model on a UK Population Based Observational Cohort

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Supplementary Tables

This Supplementary Appendix contains the information referred to the full version of this article.

Supplementary Table 1: patient characteristics

	Overall		Treated		Not treated	
	N	%	N	%	N	%
Total	271	100	217	100	54	100
Age at diagnosis (years)						
Median (Q1-Q3)	70	(59-79)	67	(57-76)	80	(75-86)
Sex						
Male	153	56.5	127	58.5	26	48.2
Female	118	43.5	90	41.5	28	51.8
International Prognostic Index (IPI)						
Low (0-1)	55	20.3	55	25.4	-	-
Low-Intermediate (2)	43	15.9	43	19.8	-	-
Intermediate-High (3)	47	17.3	43	19.8	4	7.4
High (4-5)	78	28.8	54	24.9	24	44.4
Not known	48	17.7	22	10.1	26	48.2
Age (years) >60						
Yes	194	71.6	144	66.4	50	92.6
No	77	28.4	73	33.6	4	7.4
Stage						
I	41	15.1	41	18.9	-	-
II	39	14.4	37	17.1	2	3.7
III	33	12.2	32	14.7	1	1.8
IV	132	48.7	102	47.0	30	55.6
Not fully staged	26	9.6	5	2.3	21	38.9
Extranodal Site >1						
Yes	89	32.8	69	31.8	20	37.0
No	156	57.6	142	65.4	14	26.0
CT scan not done	26	9.6	6	2.8	20	37.0
Performance status (ECOG)						
0	48	17.7	47	21.7	1	1.8
1	129	47.6	114	52.5	15	27.8
>1	94	34.7	56	21.8	38	70.4
Elevated Lactose Dehydrogenase (LDH)						
Yes	158	58.3	129	54.4	29	53.7
No	69	25.5	65	30.0	4	7.4
Not measured	44	16.2	23	10.6	21	38.9
Status at 5 years after diagnosis						
Alive	125	46.13	125	57.6	-	-
Dead	146	53.87	92	42.4	54	100
First line treatment						
Standard	161	59.41	162	74.7	-	-
Stage IA	25	9.23	25	11.5	-	-
CNS prophylaxis	23	8.49	23	10.6	-	-
CNS involvement	7	2.58	7	3.2	-	-
Not treated	54	19.9	-	-	54	100

Supplementary Table 2: Parameters for first line treatment

Regimen	CHOP	R-CHOP	R-CVP	CODOX-M/IVAC-R	IDARAM	Radiotherapy only
Treatment type						
Age ≤ 60						
% stage IA	11	89	0	0	0	0
% CNS involvement	0	20	0	20	60	0
% standard	4	96	0	0	0	0
Age 60-80						
% stage IA	8	77	0	0	0	15
% CNS involvement	0	100	0	0	0	0
% standard	5	86	9	0	0	0
Age ≥ 80						
% stage IA	0	100	0	0	0	0
% CNS involvement	0	100	0	0	0	0
% standard	4	56	28	0	0	0
Standard number of cycles	3 or 6	6 or 8	8	2	2	20 fractions
% Achieved full cycles						
Age ≤ 60	67	85	0	100	100	100
Age 60-80	20	76	44	100	100	80
Age ≥ 80	0	50	28	0	0	50
(1 st cycle) % treated as inpatient	60	39	56	100	100	0
(1 st cycle) Average (SD) LOS	22 (12)	11 (14)	9 (7)	31 (34)	37 (15)	-
(1 st cycle) Min-Max of LOS	8-48	1-68	1-20	7-55	19-68	-
(Subsequent cycles) % treated as inpatient	0	4	0	100	40	0
(Subsequent cycles) Average (SD) LOS	19 (10)	9 (12)	10 (4)	7 (2)	30 (12)	-
(Subsequent cycles) Min-Max of LOS	2-25	1-62	7-13	6-8	7-54	-
Drug cost (per cycle/per fraction)	£289	£1,730	£1,486	£6,241	£2,006	£123

* CHOP: cyclophosphamide, doxorubicin, vincristine and prednisolone

R-CHOP: cyclophosphamide, doxorubicin, vincristine and prednisolone + rituximab

R-CVP: cyclophosphamide, vincristine, prednisolone + rituximab

CODOX-M/IVAC-R: rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate + rituximab, etoposide, ifosfamide and cytarabine

IDARAM: idarubicin, dexamethasone, cytarabine, methotrexate

CNS: central nervous system

LOS: length of stay

Supplementary Table 3: Parameters for second line treatment

Regimen	R-CHOP	R-DHAP	R-ESHAP	R-CVP	R-GCVP	CODOX-M/IVAC-R	IDARAM	Radiotherapy only
Standard number of cycles	3	3	3	6	6	2	2	20 fractions
% Achieved full cycles								
Age ≤ 60	100	46	100	0	0	0	67	100
Age 60-80	0	14	100	0	0	0	00	80
Age ≥ 80	0	0	0	0	0	0	0	50
(1 st cycle) % treated as inpatient	33	39	100	0	0	100	100	0
(1 st cycle) Average (SD) LOS	4 (2)	11 (14)	17 (15)	11 (4)	12 (4)	31 (34)	37 (15)	-
(1 st cycle) Min-Max of LOS	2-6	1-68	6-28	2-15	2-14	7-55	19-68	-
(Subsequent cycles) % treated as inpatient	25	4	100	0 [†]	0 [†]	100	40	0
(Subsequent cycles) Average (SD) LOS	20 (10)	9 (12)	14 (9)	11 (4) [†]	12 (4) [†]	7 (2)	30 (12)	-
(Subsequent cycles) Min-Max of LOS	2-25	1-62	7-20	2-15 [†]	2-14 [†]	6-8	7-54	-
Drug cost (per cycle/per fraction)	£1,730	£1,952	£3,344	£1,486	£1,593	£6,241	£2,006	£123

* R-CHOP: cyclophosphamide, doxorubicin, vincristine and prednisolone + rituximab

R-DHAP: dexamethasone, cytarabine, cisplatin + rituximab

R-ESHAP: etoposide, methylprednisolone, cytarabine, cisplatin + rituximab

R-CVP: cyclophosphamide, vincristine, prednisolone + rituximab

R-GCVP: gemcitabine, cyclophosphamide, vincristine, prednisolone + rituximab

CODOX-M/IVAC-R: rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate + rituximab, etoposide, ifosfamide and cytarabine

IDARAM: idarubicin, dexamethasone, cytarabine, methotrexate

LOS: length of stay

[†] Assume the results are similar to the 1st cycle due to lack of data

Supplementary Table 4: Parameters for third line treatment

Regimen	MiniBEAM	Methotrexate
Standard number of cycles	2	2
% Achieved full cycles		
Age ≤ 60	100	80
Age 60-80	100	80
Age ≥ 80	100	50
(1 st cycle) % treated as inpatient	70	100
(1 st cycle) Average (SD) LOS	20 (8)	4 (1)
(1 st cycle) Min-Max of LOS	9-26	4-4
(Subsequent cycles) % treated as inpatient	67	100
(Subsequent cycles) Average (SD) LOS	21 (4)	4 (1)
(Subsequent cycles) Min-Max of LOS	9-30	4-4
Drug cost (per cycle)	£446	£861

* MiniBEAM: carmustine, etoposide, cytarabine, melphalan
 LOS: length of stay

Supplementary Table 5: cost items

Phases	Cost items
Diagnosis	Scans Biopsies ECG (Electrocardiography) ECHO (Echocardiograph) Blood tests
First line treatment	Chemotherapy: CHOP CHOP/R CVP/R CODOX-M/IVAC-R IDARAM Radiotherapy only Additional treatment: Methotrexate Radiotherapy Supportive care: G-CSF Transfusion Post chemotherapy imaging
Second line treatment	Chemotherapy: CHOP/R DHAP/R ESHAP/R GCVF/R CVP/R CODOX-M/IVAC-R IDARAM Radiotherapy only Additional treatment: Methotrexate Radiotherapy Supportive care: G-CSF Transfusion Post chemotherapy imaging
Third line treatment	Chemotherapy: Mini-BEAM Methotrexate Supportive care: G-CSF Transfusion Post chemotherapy imaging
Follow up	Out-patient visits Imaging if patients relapsed Biopsies if patients relapsed
End-of-life care	In-patient treatment Out-patient visits

CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone); R-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone and rituximab); R-CVP (cyclophosphamide, vincristine, prednisone and rituximab); CODOX-M/IVAC-R (cyclophosphamide, doxorubicin, vincristine, methotrexate/ifosfamide, etoposide, high dose cytarabine and rituximab); IDARAM (rituximab, idarubicin, dexamethasone, cytarabine and methotrexate); R-DHAP (dexamethasone, cytarabine, cisplatin and rituximab); R-ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin and rituximab); MiniBEAM (carmustine, etoposide, cytarabine and melphalan).

Supplementary Table 6: details of survival models

	Response after 1 st line treatment		Response after 2 nd line treatment		End of life care	
	Time to relapse	Time to death	Time to relapse	Time to death	Treated	No treated
Model type	Weibull	Exponential	Exponential	Exponential	lognormal	Lognormal
Intercept	10.73	12.31	32.36	8.49	5.76	-0.20
Age	0.09	-0.05	-0.1	-	-0.03	0.04
Time in treatment	-0.009	-	-	0.01	-	-
Had autologous stem cell transplant or not	-	-	-18.44	-	-	-
Achieved full cycle of treatment or not	-	-	-2.5	-	-	-
Shape parameter	0.60	-	-	-	-0.43	0.20

Supplementary Table 7: Comparison table of simulated and relevant study results

	Country	Price year	Patient age	Model approach	Discount rate	Time horizon	Regimen	Mean Cost (2013 UK pound *)	Mean time	Simulated cost	Simulated time
Hornberger et al.	USA	2003	>=60	Markov	3%	5 year	CHOP	\$7308 (£6394)	3.11 yrs	£7,163	1.78 yrs
							CHOP/R	\$22430 (£19485)	4.15 yrs	£20,831	3.52 yrs
Johnston et al.	Canada	2006	>15	Discrete event simulation	3%	15 year	<60				
							CHOP	\$36765 (£22713)	7.7 yrs	£14525	8.3 yrs
							CHOP/R	\$46337 (£28626)	8.3 yrs	£26761	11.8 yrs
							>60				
							CHOP	\$34968 (£21603)	4.5 yrs	£7163	1.78 yrs
							CHOP/R	\$42892 (£26498)	6.2 yrs	£20831	7.87 yrs
Knight et al.	UK	2004	Unclear	Markov	6% cost 1.5% outcome	15 year	<60				
							CHOP	£7311 (£10016)	8.86 yrs	£14525	8.3 yrs
							CHOP/R	£15181 (£20798)	9.90 yrs	£26761	11.8 yrs
							>60				
							CHOP	£5773 (£7909)	5.25 yrs	£7163	1.78 yrs
							CHOP/R	£14456 (£19805)	6.23 yrs	£20831	7.87 yrs
Best et al.	France	2003	60-80	Markov	3%	15 year	CHOP	€28782 (£28079)	4.84 yrs	£8364	2.2 yrs
							CHOP/R	€41952 (£40927)	5.83 yrs	£21596	8.58 yrs
Groot et al.	Netherlands	2002	unclear	Markov	4%	15 year	<60				
							CHOP	€27828 (£25360)	6.91 yrs	£14525	8.3 yrs
							CHOP/R	€40171 (£36609)	7.74 yrs	£26761	11.8 yrs
							>60				
							CHOP	€26891 (£24506)	4.17 yrs	£7163	1.78 yrs
							CHOP/R	€42751 (£38960)	5.14 yrs	£20831	7.87 yrs
Lee et al.	Canada	2004	21-90	Micro-costing	0%	-	CHOP:				
							1 st line	\$12240 (£7043)		£4625	
							Total	\$35292 (£20307)		£10461	
							CHOP/R				
							1 st line	\$33088 (£13897)		£15862	
							Total	\$47377 (£27261)		£23043	

* All currencies were inflated and converted to 2013 UK sterling.