Poster C21

Incremental Cost of Diffuse Large B Cell Lymphoma Beyond First-Line Therapy: A Retrospective Cohort Analysis

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BACKGROUND

- The most common subtype of non-Hodgkin lymphoma (NHL) is diffuse large B cell lymphoma (DLBCL), with approximately 28,000 estimated new cases diagnosed in 2017 in the United States[1]
- While many patients can be cured with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone),[2] about one-third will be refractory to R-CHOP or will relapse after complete response[3,4]
- Outcomes for patients with refractory DLBCL are poor, with a median overall survival (OS) of 6.3 months[5]
- This study employed a retrospective analysis of insurance claims data to examine utilization and costs associated with treating patients with DLBCL who have progressed beyond first-line (1L) therapy compared with those who never relapse
  - By understanding the magnitude and source of treatment costs, we can better estimate the economic burden of second-line (2L) therapy

METHODS

STUDY DESIGN

- Retrospective analysis of patients diagnosed with DLBCL who had received 1L R-CHOP therapy
- 2006-2015 patient-level insurance claims data from the Truven MarketScan® database were analyzed

KEY ELIGIBILITY CRITERIA

- Patients were ≥ 18 years old with R-CHOP as 1L therapy and a claim for DLBCL (ICD-9-CM 200.7X) in the year before or 90 days after 1L start were selected for 2 cohorts
  - Patients who did not relapse or received 2L treatment for ≥ 2 years
  - 2L patients with non-R-CHOP chemotherapy after 1L
- Patients who initiated 2L or subsequent therapy were analyzed based on whether hematopoietic stem cell transplant (HSCT) was received (y/n) and on time between 1L end and 2L start:
  - Early relapse (≤ 3 months)
  - Mid relapse (4 - 12 months)
  - Late relapse (> 12 months)
- Patients not continuously enrolled for 6 months before and ≥ 2 years after 1L initiation, or those treated with maintenance rituximab or lenalidomide were excluded

ASSESSMENTS

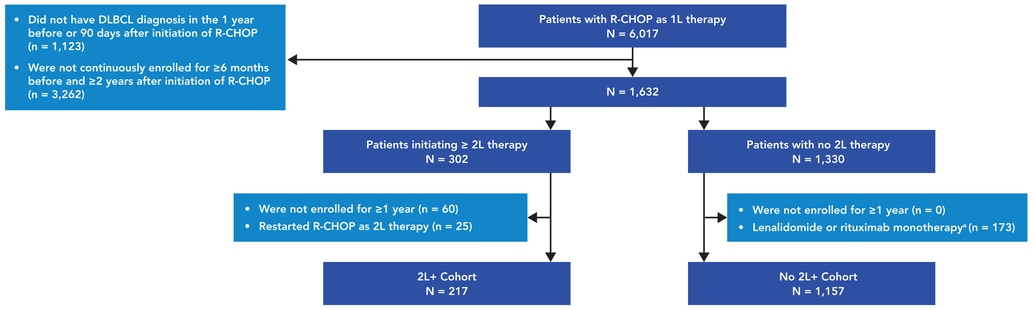
- 1- and 2-year hospitalization rate, length of stay, and HSCT rate
- 1- and 2-year unadjusted costs (total, inpatient, outpatient, pharmacy, and chemotherapy-related)
- 1-, 2-, and 3-year total costs according to length of enrollment
- Baseline demographic and comorbidity measures

ANALYSES

- Descriptive statistics compared use and costs between groups
- Multivariate analyses estimated 1- and 2-year costs, adjusted for age, gender, region, comorbidities
- Healthcare costs were adjusted to 2015 United States dollar (USD) based on Consumer Price Index for Health Services

RESULTS

Figure 1. Patient Selection



1L, first-line; 2L, second-line; DLBCL, diffuse large B cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
[a]Excluded as it was not possible to differentiate treatment from maintenance in the claims database.

Table 1. Patient Demographics and Comorbidities

	2L+ Therapy			Timing of Relapse				HSCT Status		
	2L+ N = 217	No 2L+ N = 1157	*P* Value	Early Relapse N = 87	Mid Relapse N = 66	Late Relapse N = 64	*P* Value	HSCT N = 61	No HSCT N = 156	*P* Value
Mean age (SD), years	58.3 (14.1)	60.8 (14.4)	.020	55.5 (15.8)	58.3 (13.5)	62.1 (11.4)	.014	54.7 (10.9)	59.7 (15.0)	.007
Female, n (%)	90 (41.5)	541 (46.8)	.152	42 (48.3)	22 (33.3)	26 (40.6)	.176	20 (32.8)	70 (44.9)	.104
Region, n (%)										
Midwest	69 (31.8)	392 (33.9)	.017	26 (29.9)	19 (28.8)	24 (37.5)	.452	20 (32.8)	49 (31.4)	.862
Northeast	51 (23.5)	190 (16.4)		25 (28.7)	14 (21.2)	12 (18.8)		13 (21.3)	38 (24.4)	
South	74 (34.1)	379 (32.8)		25 (28.7)	28 (42.4)	21 (32.8)		20 (32.8)	54 (34.6)	
West	23 (10.6)	196 (16.9)		11 (12.6)	5 (7.6)	7 (10.9)		8 (13.1)	15 (9.6)	
Payment source, n (%)										
Commercial	149 (68.7)	716 (61.9)	.058	61 (70.1)	47 (71.2)	41 (64.1)	.633	51 (83.6)	98 (62.8)	.003
Medicare	68 (31.3)	441 (38.1)		26 (29.9)	19 (28.8)	23 (35.9)		10 (16.4)	58 (37.2)	
Mean Charlson Comorbidity Index (SD)	4.2 (3.0)	3.8 (2.6)	.039	5.0 (3.6)	3.6 (2.6)	3.8 (2.3)	.007	3.6 (2.6)	4.5 (3.2)	.051
Mean Chronic Condition Indicator (SD)	4.7 (1.9)	4.6 (1.9)	.370	5.5 (1.8)	4.5 (1.8)	3.9 (1.7)	< .001	4.0 (1.6)	5.0 (2.0)	< .001

2L, second-line; HSCT, hematopoietic stem cell transplant; SD, standard deviation.

- The median follow-up time for the 2L+ and no 2L+ patients groups was 30 and 38.4 months, respectively

Table 2. Unadjusted 1-Year Healthcare Utilization and Costs

	2L+ Therapy			Timing of Relapse				HSCT Status		
	2L+ N = 217	No 2L+ N = 1157	*P* Value	Early Relapse N = 87	Mid Relapse N = 66	Late Relapse N = 64	*P* Value	HSCT N = 61	No HSCT N = 156	*P* Value
Any inpatient hospitalization, n (%)	173 (79.7)	176 (15.2)	< .001	68 (78.2)	55 (83.3)	50 (78.1)	.682	61 (100.0)	112 (71.8)	< .001
Mean number of hospitalizations (SD)	2.7 (2.6)	0.2 (0.6)	< .001	2.7 (2.4)	2.8 (2.8)	2.5 (2.7)	.854	3.3 (2.4)	2.4 (2.7)	.019
Mean length of stay (SD), days	23.1 (22.0)	7.4 (12.6)	< .001	19.5 (17.4)	28.2 (26.3)	22.3 (21.9)	.089	32.3 (17.5)	12.9 (20.9)	< .001
HSCT within 1 year, n (%)	61 (28.1)	0 (0)	< .001	20 (23.0)	26 (39.4)	15 (23.4)	.050	–	–	–
Total healthcare costs, USD										
Mean (SD)	210,488 (172,851)	25,044 (32,441)	< .001	191,079 (175,752)	232,796 (164,914)	213,866 (176,517)	.331	301,426 (174,320)	174,928 (159,203)	< .001
Median	160,483	15,372		130,929	200,305	161,465		238,032	116,223	
Mean inpatient costs (SD), USD	90,882 (109,480)	4,421 (16,602)	< .001	83,345 (107,479)	109,865 (114,420)	81,551 (106,176)	.240	168,998 (102,761)	60,337 (96,305)	.019
Chemotherapy[a]	23,743 (41,911)	0 (0)	< .001	25,395 (43,613)	23,498 (44,608)	21,750 (36,945)	.869	26,771 (38,681)	22,559 (43,169)	.507
HSCT[b]	35,428 (68,905)	0 (0)	< .001	32,104 (76,278)	49,933 (74,121)	24,987 (48,182)	.100	126,030 (74,052)	0 (0)	< .001
Mean outpatient costs (SD), USD	109,525 (92,980)	17,686 (19,850)	< .001	98,553 (88,696)	112,076 (85,710)	121,810 (104,862)	.306	118,083 (96,783)	106,178 (91,551)	.398
Office visits	34,035 (44,972)	5,405 (6,437)	< .001	31,802 (44,972)	33,682 (40,102)	37,433 (44,135)	.748	26,813 (31,932)	36,858 (48,940)	.078
Hospital visits	66,632 (82,313)	10,089 (16,380)	< .001	59,963 (82,632)	69,464 (77,462)	72,778 (100,525)	.607	85,269 (88,945)	59,345 (78,673)	.037
Emergency room visits	529 (3,081)	267 (1,783)	.225	405 (1,022)	848 (5,402)	369 (919)	.602	306 (609)	616 (3,613)	.302
Other	8,329 (27,631)	1,925 (7,058)	< .001	6,382 (15,279)	8,081 (34,528)	11,230 (32,480)	.567	5,694 (9,599)	9,359 (32,007)	.199
Chemotherapy	23,280 (30,219)	0 (0)	< .001	21,366 (27,602)	22,361 (26,554)	26,828 (36,672)	.526	18,088 (23,766)	25,309 (32,237)	.072
Mean pharmacy costs (SD), USD	10,081 (13,919)	2,937 (7,776)	< .001	9,182 (13,286)	10,854 (14,693)	10,505 (14,092)	.733	14,345 (15,436)	8,413 (12,953)	.005
Chemotherapy	220 (1,108)	0 (0)	< .001	92 (676)	499 (1,742)	105 (583)	.048	69 (436)	279 (1,275)	.073

2L, second-line; DRG, diagnostic-related group; HSCT, hematopoietic stem cell transplant; SD, standard deviation.
[a]Based on DRG indicators in claims. Specific charges for chemotherapy or HSCT cannot be identified through inpatient claims. Chemotherapy DRG includes associated procedures, drugs, and materials, etc., and in some instances, may include the cost related to HSCT (e.g., for conditioning regimens).

Table 3. Unadjusted 2-Year Healthcare Utilization and Costs

	2L+ Therapy			Timing of Relapse				HSCT Status		
	2L+ N = 153	No 2L+ N = 961	*P* Value	Early Relapse N = 83	Mid Relapse N = 33	Late Relapse N = 37	*P* Value	HSCT N = 44	No HSCT N = 109	*P* Value
Any inpatient hospitalization, n (%)	124 (81.0)	203 (21.1)	< .001	66 (79.5)	27 (81.8)	31 (83.8)	.852	44 (100.0)	80 (73.4)	< .001
Mean number of hospitalizations (SD)	3.8 (2.8)	0.3 (0.9)	< .001	4.0 (2.7)	3.6 (3.1)	3.5 (2.9)	.878	4.1 (2.9)	3.6 (2.8)	.393
Mean length of stay (SD), days	23.9 (23.4)	8.4 (18.5)	< .001	22.1 (22.3)	29.4 (24.9)	23.0 (24.4)	.382	35.7 (23.5)	17.4 (20.9)	< .001
HSCT within 1 year, n (%)	44 (29)	0	< .001	18 (22)	15 (45)	11 (30)	.038	–	–	–
Total healthcare costs, USD										
Mean (SD)	267,770 (266,536)	42,272 (49,281)	< .001	264,900 (300,924)	280,876 (229,577)	262,520 (215,949)	.950	421,739 (363,498)	205,618 (183,901)	< .001
Median	186,944	28,059		150,421	212,968	225,218		291,944	145,895	
Mean inpatient costs (SD), USD	105,503 (144,188)	7,047 (27,326)	< .001	106,511 (165,722)	115,131 (121,291)	94,655 (109,263)	.837	215,860 (183,414)	60,956 (94,348)	< .001
Chemotherapy[a]	23,416 (42,551)	0 (0)	< .001	26,969 (47,709)	17,667 (32,859)	20,575 (37,850)	.513	33,635 (48,732)	19,291 (39,280)	.059
HSCT[b]	40,981 (82,861)	0 (0)	< .001	37,177 (91,727)	60,487 (85,098)	32,118 (54,080)	.299	142,504 (97,296)	0 0	< .001
Mean outpatient costs (SD), USD	145,952 (144,548)	29,462 (30,788)	< .001	143,042 (154,205)	144,979 (123,412)	153,347 (142,973)	.937	183,686 (200,214)	130,720 (112,393)	.104
Office visits	43,281 (62,029)	9,220 (10,997)	< .001	43,275 (67,993)	36,092 (44,425)	49,704 (62,219)	.660	34,697 (46,986)	46,746 (67,037)	.210
Hospital visits	88,871 (112,723)	16,476 (25,229)	< .001	88,348 (117,193)	90,887 (105,264)	88,244 (111,857)	.993	134,977 (156,296)	70,259 (83,315)	.012
Emergency room visits	847 (2,270)	525 (2,924)	.120	1,124 (2,876)	452 (1,069)	577 (1,225)	.253	662 (1,393)	921 (2,541)	.421
Other	13,022 (41,955)	3,241 (9,868)	.004	10,414 (29,604)	17,558 (66,279)	14,826 (38,642)	.682	13,533 (34,846)	12,815 (44,652)	.924
Chemotherapy[b]	29,024 (41,568)	0 (0)	< .001	29,375 (41,517)	18,645 (21,811)	37,495 (52,666)	.166	21,878 (31,860)	31,909 (44,705)	.122
Mean pharmacy costs (SD), USD	16,315 (24,268)	5,292 (8,659)	< .001	15,346 (25,140)	20,766 (24,104)	14,518 (22,513)	.488	22,193 (28,035)	13,942 (22,275)	.057
Chemotherapy	935 (6,164)	0 (0)	< .001	913 (7,277)	1,853 (6,525)	164 (766)	.522	2,273 (10,938)	395 (2,196)	.265

2L, second-line; DRG, diagnostic-related group; HSCT, hematopoietic stem cell transplant; SD, standard deviation.
[a]Based on DRG indicators in claims. Specific charges for chemotherapy or HSCT cannot be identified through inpatient claims. Chemotherapy DRG includes associated procedures, drugs, and materials, etc., and in some instances, may include the cost related to HSCT (e.g., for conditioning regimens).
[b]Cost of chemotherapy administration may be charged on separate outpatient claims from those that include chemotherapy agents. For example, all chemotherapy agents during an outpatient hospital stay (or other outpatient location) may be billed on a separate outpatient claim that does not include any chemotherapy procedures.

- 2L+ patients had significantly higher costs and more frequent and longer hospitalizations than patients without 2L+ treatment (**Tables 2 and 3, left**)
  - The mean length of hospitalization stay was approximately 3x longer for 2L+ vs the no 2L+ cohort in both years 1 and 2 (year 1: 23.1 vs 7.4 days, $P < 0.001$; year 2: 23.9 vs 8.4 days, $P < 0.001$)
  - The total mean healthcare costs for 2L+ patients was more than 8-fold greater in year 1 and 6-fold greater in year 2 than that of patients who did not receive 2L+ ($P < 0.001$)
- There was no significant difference in hospitalization or costs between patients with early, mid, and late relapse (**Tables 2 and 3, middle**)
- Significantly different proportions of early vs mid vs late relapse patients underwent HSCT within one year in year 1 (23% vs 39% vs 23%; $P = .05$) and in year 2 (22% vs 45% vs 30% $P = .038$)
- While HSCT vs no HSCT patients had similar mean outpatient costs (year 1: $118,083 vs $106,178, $P = .398$; year 2: $183,686 vs $130,720; $P = .0104$; **Tables 2 and 3, right**), patients who received HSCT had significantly higher inpatient costs and overall costs

Table 4. Adjusted 1-Year and 2-Year Total Healthcare Costs[a]

	2L+ Therapy			Timing of Relapse				HSCT Status		
	2L+	No 2L+	*P* Value	Early Relapse	Mid Relapse	Late Relapse	*P* Value	HSCT	No HSCT	*P* Value
Mean total 1-year costs (95% CI),[b] USD	N = 217 208,300 (198,396 - 218,204)	N = 1157 25,454 (21,189 - 29,719)	< .001	N = 87 195,500 (161,782 - 229,218)	N = 66 213,993 (175,587 - 252,400)	N = 64 227,247 (188,072 - 266,421)	0.487	N = 61 282,022 (241,594 - 322,450)	N = 156 182,516 (157,803 - 207,229)	< .001
Mean total 2-year costs (95% CI),[b] USD	N = 153 257,822 (260,872 - 290,772)	N = 961 43,092 (36,654 - 49,530)	< .001	N = 83 270,013 (214,764 - 325,262)	N = 33 $240,295 (152934 - 327655)	N = 37 287,244 (202139 - 372349)	0.744	N = 44 409,778 (333259 - 486296)	N = 109 210,446 (163258 - 257635)	< .001

2L, second-line; HSCT, hematopoietic stem cell transplant; SD, standard deviation.
[a]Mean total healthcare costs adjusted by age group, gender, region, Charlson Comorbidity Index. Comparisons between response types were further adjusted for HSCT in the first year after start of second-line treatment. Comparisons between HSCT statuses were further adjusted for timing of relapse.
[b]2-year adjusted costs were calculated. These analyses were performed for exploratory purposes, the results of which may not be interpretable due to insufficient sample size.

- Total 1- and 2-year costs were significantly higher for patients who received 2L+ treatment vs no treatment ($P < .001$; **Table 4**)
  - 2L+ patients who received HSCT vs no HSCT had significantly higher 1-year and 2-year costs
  - Timing of relapse did not significantly impact 1-year or 2-year costs

Table 5. Cost Over Time Among Patients on 2L+ Treatment

	1 Year of Enrollment	2 Years of Enrollment	3 Years of Enrollment
Mean total costs (SD), USD	2L+ cohort N = 64	2L+ cohort N = 73	2L+ cohort N = 79
Year 1	233,593 (174,946)	229,566 (198,500)	172,937 (139,009)
Year 2	–	99,113 (179,311)	37,771 (66,243)
Year 3	–	–	37,486 (57,842)

2L, second-line; SD, standard deviation.

- For patients with 2 or 3 years of treatment, costs decrease from year 1 (**Table 5**)
  - Short time on treatment may be indicative of early death[5]

CONCLUSIONS

- While these data do not fully account for all factors, such as disease severity, which may contribute to bias in the estimates, these data demonstrate that treatment of DLBCL is resource intensive beyond 1L treatment, with 8-fold greater 1-year costs for patients who initiated 2L+ treatment vs those who did not
- HSCT is a major driver of cost despite occurring in fewer than one-third (28%) of 2L+ patients
  - This may explain the trend for higher costs among mid-relapse patients as this group was more likely to undergo HSCT
  - Curative transplants are not frequently utilized and few relapsed patients undergo HSCT (28%)
- Chemotherapy is another major contributor of costs, accounting for over one-fifth of total costs
- Additional studies that focus on only patients with 2L+ treatment may result in a larger sample size and greater ability to detect cost differences within 2L+ patients over multiple years
- Emergence of effective therapies in the 2L+ setting that prevent the need for expensive transplants may save costs

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DISCLOSURES

AP: Employment Kite Pharma; **RT, SRR, MSB:** Consultant for Kite Pharma.