ECONOMIC BURDEN ASSOCIATED WITH AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: A NATIONWIDE HEALTH INSURANCE CLAIMS DATABASE STUDY IN JAPAN DURING 2012-2022

Saaya Tsutsué[**1]; Shinichi Makita[2]; Hiroya Asou[**3]; Shingo Wada[4]; Wen Shi Lee[4]; Dilinuer Ainiwaer[4]; Koki Idehara[4]; Sona-Sanae Aoyagi[4]; Seok-Won Kim[4]

1 Kite Value & Access, Gilead Sciences Japan, Tokyo, Japan; 2 National Cancer Center Hospital, Tokyo, Japan; 3 Kite Clinical Development, Gilead Sciences Japan, Tokyo, Japan; 4 IQVIA Solutions Japan, Tokyo, Japan

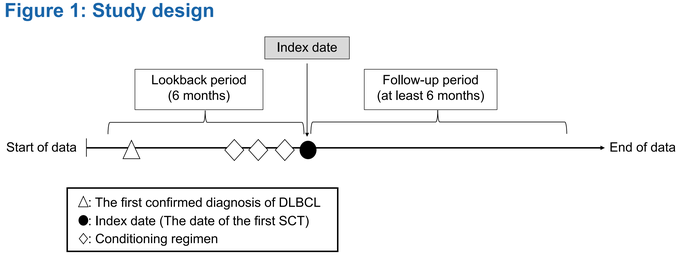
***ASH international member*

INTRODUCTION & AIM

- Globally, non-Hodgkin lymphomas (NHL) are the most pervasive hematological malignancies. Among NHLs, diffuse large B-cell lymphoma (DLBCL) is the most prevalent subtype worldwide, accounting for 35.8% of all subtypes of NHL in Japan.[1,2]
- The Japanese clinical guidelines recommend treatment with high-dose salvage chemotherapy and autologous stem cell transplantation (ASCT) in transplant eligible, chemotherapy-sensitive relapsed/refractory patients.
- To fully capture continuous follow-up data of DLBCL patients and cost drivers associated with treatment for those who received ASCT in Japan, this study was conducted using universal co-payment Japanese health insurance association (HIA) claims database to reveal potential cost drivers and driving factors of direct healthcare costs in patients with DLBCL receiving stem cell transplantation (SCT).

METHODS

Figure 1: Study design



Study design and population

- This is a retrospective observational study of DLBCL patients who received SCT using the Medical Data Vision, Co. Ltd. (MDV; Tokyo, Japan) HIA claims database from April 2012 to August 2022 inclusive, with the index date being that of the first SCT.
- Patients eligible for this study were selected based on these inclusion criteria: 1) Had a confirmed diagnosis of DLBCL based on the ICD-10 at least one time during the whole study period; 2) Received allo-SCT or ASCT on or after the month of the first confirmed diagnosis of DLBCL; 3) Received high-dose chemotherapy (conditioning regimen) during the 6-month lookback period. Exclusion criteria were: 1) Received CAR-T drug before the index date; 2) Did not have a 6-month lookback period; 3) Did not have at least a 6-month follow-up period. An overview of the analysis design is presented in Figure 1.

Statistical analysis

- Structural equation modeling (SEM) analysis was conducted to identify factors related to SCT treatment costs in DLBCL. Direct effects, indirect effects, and total effects were evaluated in the model.

CONTACT INFORMATION

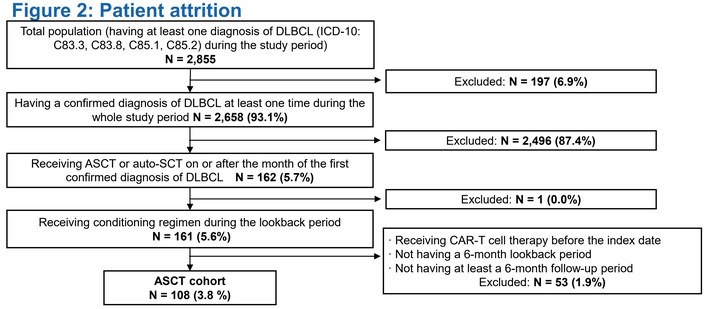
Corresponding author:

- Saaya Tsutsué, PhD, Gilead Sciences, Japan
  Saaya.Tsutsue@gilead.com

RESULTS

- A total of 108 patients (3.8%) among all DLBCL patients who received SCT met the eligibility criteria and were considered ASCT patients. The cohort disposition process is presented in Figure 2. Patient characteristics along with subsequent therapies are provided in Tables 1a & 1b, respectively.
- The median (Q1, Q3) of the total cost for ASCT patients during the lookback and follow-up period was $78,718.63 ($57,175.90, $141,108.38) in Table 1c.

Figure 2: Patient attrition



Abbreviations: ASCT, Allogenic stem cell transplantation; Auto-SCT, Autologous stem cell transplantation; CAR-T, Chimeric antigen receptor T-cell; DLBCL, Diffuse large B-cell lymphoma; SCT, Stem cell transplantation

Table 1a: Patient characteristics

Patient characteristics	N=108
Gender n (%)	
Male, Female	63 (58.3), 45 (41.7)
Age at index date	
Median (Q1, Q3)	55 (48, 58)
Age groups n (%)	
18 - 65 years	105 (97.2)
≥ 66 years	3 (2.8)
Index year groups n (%)	
2012 – 2019	74 (68.5)
2020 – 2022	34 (31.5)
Length of follow-up period (days)	
Median (Q1, Q3)	686.5 (397.5, 1275.5)
Modified CCI score categories n (%)	
0-2	14 (13.0)
3-4	45 (41.7)
5+	49 (45.4)
Complications n (%)	
Heart disease	4 (3.7)
Kidney disease	2 (1.8)
Liver disease	8 (7.41)

HCRU	Mean (SD)	Median (Q1, Q3)
LOS of SCT-related hospitalization	36.88 (12.95)	34.00 (28.50, 42.00)
Frequency of follow-up hospitalization on/after SCT-related hospitalization	1.66 (1.36)	1.00 (1.00, 2.00)

Table 1b: Subsequent therapies

Subsequent therapies	n (%)
R+/-DeVIC-based	4 (3.7)
R-CHASE-based	2 (1.8)
GDP-based with or without R	8 (7.4)
R-bendamustine-based	1 (0.9)
R-EPOCH, DA-EPOCH, DA-EPOCH-R	2 (1.8)
R+/-ESHAP-based	2 (1.8)
R-ICE-based	1 (0.9)
R-DHAP-based	0 (0.0)
Pola-BR	2 (1.8)
Pola-R-CHP	0 (0.0)
CAR-T cell therapy	2 (1.8)

Abbreviations: CAR-T cell, Chimeric antigen receptor T cell; CCI, Charlson Comorbidity Index; CHASE, Cyclophosphamide, cytarabine, etoposide, dexamethasone; DA, Dose-adjusted; DeVIC, Dexamethasone, etoposide, ifosfamide, carboplatin; DHAP, Dexamethasone, cytarabine, cisplatin; ESHAP, Etoposide, cytarabine, cisplatin, methylprednisolone; EPOCH, Etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin; GDP, Gemcitabine, dexamethasone, cisplatin/carboplatin; SD, Standard deviation; ICE, Ifosfamide, carboplatin, etoposide; Pola-BR, Polatuzumab vedotin, bendamustine, and rituximab; Pola-R-CHP, Polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, and prednisone; R, Rituximab

Table 1c: ASCT Cost

ASCT Cost (Adjusted for 2022 price index)		Median	Q1, Q3
Total	N = 51	$78,718.63	$57,175.90, $141,108.38
Lookback	N = 108	$9,771.93	$7,772.13, $13,634.66
Follow-up	0 to 6 months (N = 108)	$53,263.95	$37,514.37, $71,732.11
	7 to 12 months (N = 88)	$2,015.07	$1,225.85, $8,380.83
	13 to 24 months (N = 51)	$3,395.42	$1,909.02, $8,133.96

The unit prices were adjusted to those as of April 2022 by the revision rates of the biannual medical service fee and drug price revisions (which were accounted for inflation as well as global health care budget), in line with Japanese HTA C2H guidelines with following USD conversion method from previous study. [4,5]

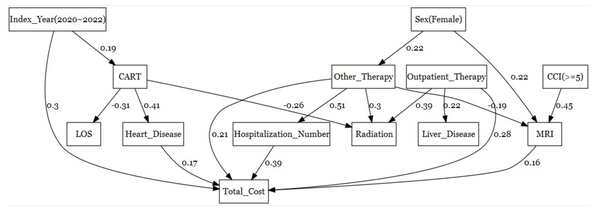
Table 2: Direct, indirect, and total effects on healthcare cost obtained from model (best-fit model)

Total healthcare cost drivers	N=108	Direct effects (USD)			Indirect effects (USD)			Total effects (USD)		
	n (%)	β	95% CI	p	β	95% CI	p	β	95% CI	p
Patient characteristics										
Gender (reference: male)										
Female	45 (41.67)	-0.079	-0.234, 0.075	0.313	0.118	-0.006, 0.242	0.061	0.039	-0.143, 0.221	0.676
Age (reference: 18-65 years)										
≥ 66 years	3 (2.78)	-0.002	-0.151, 0.147	0.976	-0.060	-0.178, 0.057	0.315	-0.062	-0.245, 0.120	0.502
Index year (reference: 2012-2019)										
2020 – 2022	34 (31.48)	0.299	0.148, 0.450	0.000	-0.110	-0.240, 0.019	0.095	0.188	0.009, 0.368	**0.039**
Comorbidities										
CCI score (reference: 0-2)										
3	17 (15.74)	-0.001	-0.207, 0.205	0.995	0.090	-0.074, 0.254	0.283	0.089	-0.158, 0.336	0.479
4	28 (25.93)	0.149	-0.073, 0.371	0.188	0.050	-0.126, 0.227	0.579	0.199	-0.069, 0.468	0.146
5+	49 (45.37)	0.174	-0.078, 0.427	0.175	0.180	-0.020, 0.381	0.078	0.355	0.069, 0.641	**0.015**
Prior/concurrent non-lymphoma neoplasms^										
Yes	66 (61.11)	-0.079	-0.238, 0.079	0.326	0.020	-0.108, 0.148	0.759	-0.059	-0.250, 0.132	0.542
Complications										
Heart disease^	4 (3.70)	0.174	0.013, 0.334	0.034	-	-	-	0.174	0.013, 0.334	**0.034**
Kidney disease^	2 (1.85)	0.031	-0.115, 0.176	0.678	-	-	-	0.031	-0.115, 0.176	0.678
Liver disease^	8 (7.41)	-0.056	-0.204, 0.092	0.459	-	-	-	-0.056	-0.204, 0.092	0.459
Chemotherapy regimen post SCT†										
Outpatient regimen	9 (8.33)	0.285	0.121, 0.448	0.001	-0.067	-0.182, 0.048	0.252	0.217	0.055, 0.379	**0.009**
CAR-T cell therapy	2 (1.85)	0.026	-0.150, 0.202	0.775	0.121	-0.006, 0.248	0.061	0.147	-0.020, 0.313	0.084
Other regimen	8 (7.41)	0.206	0.019, 0.392	0.031	0.122	-0.016, 0.261	0.083	0.328	0.164, 0.493	**0.000**
HCRU										
Number of hospitalizations	-	0.389	0.222, 0.555	0.000	-	-	-	0.389	0.222, 0.555	**0.000**
Any ICU admission*^	0 (0.00)	-	-	-	-	-	-	-	-	-
Any PET scans	3 (2.78)	-0.005	-0.152, 0.143	0.949	-	-	-	-0.005	-0.152, 0.143	0.949
Any MRI scans	12 (11.11)	0.161	0.003, 0.318	0.046	-	-	-	0.161	0.003, 0.318	0.046
Any CT scans	55 (50.93)	-0.053	-0.205, 0.099	0.494	-	-	-	-0.053	-0.205, 0.099	0.494
Any ER visits*	0 (0.00)	-	-	-	-	-	-	-	-	-
Any RT	1 (0.93)	-0.127	-0.302, 0.047	0.153	-	-	-	-0.127	-0.302, 0.047	0.153
LOS**	-	0.133	-0.022, 0.288	0.093	-	-	-	0.133	-0.022, 0.288	0.093
Standardized Root Mean Square Residual (SRMR)										0.077‡

Abbreviations: CAR-T, Chimeric antigen receptor T-cell; CCI, Charlson comorbidity index; CI, Confidence interval; CT, Computed tomography; ER, Emergency room; HCRU, Healthcare resource utilization; ICU, Intensive care unit; LOS, Length of hospital stay; MRI, Magnetic resonance imaging; PET, Positron emission tomography; RT: Radiation therapies; SCT, Stem cell transplant; SD, Standard deviation; Note: ^No reference; *No variance in the variable; therefore, no effects observed, **Log link has been applied for total healthcare costs in SEM, †Grouping subsequent therapy in the full model (for example, if there is any one of DEVIC, CHASE, or CAR-T it will be included in the model with Therapy=1.)
‡ Important criteria for assessing goodness-of-fit model in SEM based on the standardized root mean squared residual (SRMR < 0.08).

- Factors displaying statistically significant direct effects include index year “from 2020 to 2022” (baseline was “from 2012 to 2019”) , heart disease as a complication, and outpatient regimen. Other prime cost drivers imposing direct effects were other regimens as subsequent therapy, and MRI scan during first ASCT hospitalization as presented in Table 2.

Figure 3: SEM path analysis for cost drivers representing statistically significant effects of direct & indirect paths



- The model coefficients for the total, direct, and indirect effects on the total healthcare costs are presented in Table 2, while Figure 3 presents the significant factors of the model through path diagram.
- The number of hospitalizations including ASCT related hospitalization and post-ASCT regimens had the greatest impact on the total health care costs.

CONCLUSIONS

- This is the first study to examine the total cost and healthcare resource use of ASCT among patients with DLBCL in a nationwide setting with a follow-up period of up to 24 months and will become a benchmark when considering new innovative therapies for patients with DLBCL in Japan from the aspect of healthcare economics of patient care.
- This study also identified the cost drivers of ASCT-related costs for DLBCL patients which may be a future insight and reference to consider optimized care for patients under the nationwide universal health insurance coverage in Japan.
- Total healthcare cost is majorly impacted due to the number of hospitalizations including ASCT related hospitalization. CCI score (≥5) and receiving “other” regimens post ASCT were major key drivers of the total healthcare cost.
- Other total healthcare cost drivers including heart disease complication are consistent with the previous study[4] targeting salvage chemotherapies and SCT in patients with DLBCL in Japan.

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- This study was funded by Gilead Sciences.