Treatment preferences among patients with relapsed or refractory diffuse large B-cell lymphoma in France, Germany, Italy, Japan, Spain, the United States, and the United Kingdom

PCR236

Christine Michaels-Igbokwe, PhD,[1] Hannah Collacott, MSc,[2] Harrison Clarke, MSc,[2] Fei Fei Liu, MBA[3]

[1]Evidera PPD, Montreal, QC, Canada; [2]Evidera PPD, Bethesda, MD, USA; [3]Bristol Myers Squibb, Princeton, NJ, USA

Introduction

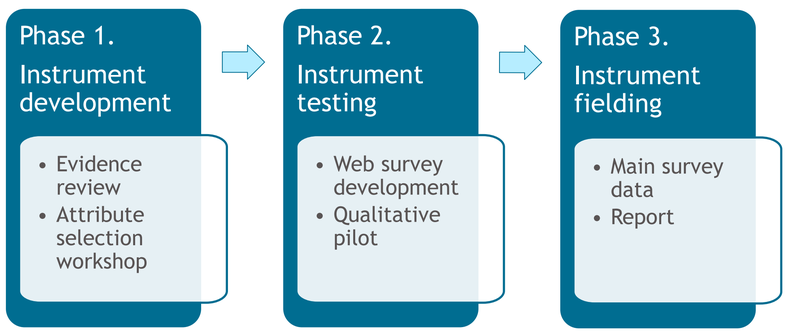
- Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL) type, which accounts for about one-third of NHL cases in the United States (US),[1] 58% of cases in the United Kingdom (UK),[2] and ~45% of cases in Japan[3]
- As the number of treatment options for relapsed or refractory (R/R) DLBCL expands, it is important to understand how patients value different treatment options
- Quantitative data on patient preferences generated using stated preference research methods can provide unique insights into the relative importance of treatment benefit and risks, and help to understand the role of nonclinical attributes in influencing treatment preferences[4,5]
- The present study used a best-best scaling discrete choice experiment (BBS-DCE) to quantify patient preferences for R/R large B-cell lymphoma (LBCL) treatments

Objectives

- Identify the key attributes that differentiate existing therapies available for patients with LBCL that would influence their treatment preferences
- Elicit and quantify patients' preferences for key factors differentiating available treatments for LBCL (eg, benefit-risk trade-offs)
- Understand how these preferences vary within the target population (eg, based on age, gender, risk level, treatment experience, and treatment understanding)

Methods

Figure 1. Study flow diagram



- An online/web-based BBS-DCE survey was developed (**Figure 1**) and administered to adults with self-reported R/R LBCL in Europe, Japan, and the US who were either transplant-eligible or non-eligible for second-line (2L) treatment or in third-line or later (3L+) treatment
- LBCL diagnoses were self-confirmed, and a screening questionnaire was used to ascertain disease status
- Nine experimentally designed BBS-DCE tasks consisted of 3 hypothetical treatment profiles, including 2 experimental profiles and a fixed profile representing standard of care (SOC; ie, non–chimeric antigen receptor [CAR T] cell therapy)
- Treatment attributes included 2-year progression-free survival (PFS), acute treatment reaction (cytokine release syndrome, neurological events), serious infections, chronic adverse effects, dosing schedule, and administration location

Table 1. Final attributes and levels

Attribute name	Attribute descriptions	Levels
Treatment success	The chance of surviving and being in remission 2 years after starting treatment. How well treatments work is measured by how well the cancer responds to treatment. A good response usually means patients will survive longer and achieve remission (ie, they no longer experience cancer symptoms or require treatment)	1. 5 out of 100 (5%) 2. 25 out of 100 (25%) 3. 45 out of 100 (45%)
Dosing schedule	The way in which patients receive treatment. Treatments are administered in 1 cycle or across multiple cycles to maximize the chance of working. Treatment cycles typically last 21–28 days. For treatments requiring 1 cycle, no further treatment is required until disease progression, and patients switch to a new treatment (a hospital visit would be required for each cycle)	1. Single-cycle treatment 2. Multicycle treatment for 6 months 3. Multicycle treatment, continuous until disease progression
Location of administration	This refers to where patients receive treatment. Different treatments are administered by different clinicians and in different practice settings. If not administered in a local hospital, patients would need to travel to receive treatment and may need to stay close to the hospital for multiple appointments	1. Local hospital 2. Nonlocal hospital
Risk of acute treatment reaction	The patient's risk of experiencing an acute reaction within 2 weeks of the treatment being administered. Acute reactions include cytokine release syndrome and neurological events, which can be life-threatening. Symptoms include high fever, fatigue, nausea, organ failure, confusion, headaches, and seizures	1. 0 out of 100 (0%) 2. 15 out of 100 (15%) 3. 35 out of 100 (35%)
Chronic side effects while on treatment	The severity of chronic side effects that patients experience as a result of treatment that lasts for the duration patients are receiving treatment. When chronic side effects are mild, no treatment is required and there is no impact on daily activities; when moderate, patients need to take other medicines to manage them and there is a moderate impact on daily activities. Examples of chronic side effects include nausea and vomiting, fatigue, headaches, and confusion	1. No chronic side effects 2. Mild chronic side effects 3. Moderate chronic side effects
Risk of experiencing serious infections	The risk of experiencing serious infections can be a side effect of some treatments. Some treatments can compromise the patient's immune system and increase risk of catching serious infections, which can be life-threatening. Common serious infections include pneumonia, urinary tract infections, and shingles	1. 0 out of 100 (0%) 2. 10 out of 100 (10%) 3. 30 out of 100 (30%)

- Final attribute descriptions and levels can be found in **Table 1**

Results

- Of 500 patients invited to participate in the survey, 258 were screened, 219 were considered eligible to participate, and 210 completed the survey
  - Reasons for study exclusion of the 39 patients included: not diagnosed with eligible condition (n = 1), not diagnosed with blood cancer (n = 1), type of blood cancer (n = 6), type or grade of cancer (n = 3), still on first-line (1L) treatment or unaware of current line (n = 9), 1L treatment worked or will not switch treatment (n = 8), and study full (n = 11)

Table 2. Patient demographics and disease characteristics

Characteristics	Overall (n = 210)	US (n = 95)	UK (n = 24)	Italy (n = 26)	Germany (n = 25)	Spain (n = 11)	France (n = 9)	Japan (n = 20)
Proportion of sample, %	–	45.2	11.4	12.4	11.9	5.2	4.3	9.5
Age, y								
Mean (SD)	58.8 (11.3)	61.0 (7.8)	51.0 (14.3)	60.2 (9.5)	55.4 (12.9)	49.8 (13.8)	69.4 (12.6)	60.4 (11.2)
Median (IQR)	60 (52–66)	63 (56–67)	52 (42–60)	62 (55–66)	51 (48–62)	54 (42–58)	65 (62–75)	64 (58–67)
Age group, n (%)								
18–34 y	9 (4.3)	0	4 (16.7)	1 (3.9)	1 (4.0)	1 (9.1)	0	2 (10.0)
35–64 y	127 (60.5)	56 (59.0)	15 (62.5)	15 (57.7)	19 (76.0)	9 (81.8)	4 (44.4)	9 (45.0)
≥ 65 y	74 (35.2)	39 (41.1)	5 (20.8)	10 (38.5)	5 (20.0)	1 (9.1)	5 (55.6)	9 (45.0)
Sex, n (%)								
Male	112 (53.3)	50 (52.6)	9 (37.5)	20 (76.9)	14 (56.0)	5 (45.5)	3 (33.3)	11 (55.0)
Insurance status (US and Japan),[a] n (%)								
Employer-provided insurance (US)/social health insurance (Japan)	16 (7.6)	14 (14.7)	0	0	0	0	0	2 (10.0)
Self-provided insurance (US)/private insurance (Japan)	35 (16.7)	34 (35.8)	0	0	0	0	0	1 (5.0)
National health insurance (Japan)	17 (8.1)	0	0	0	0	0	0	17 (85.0)
Veterans affairs/military health care (US)	14 (6.7)	14 (14.7)	0	0	0	0	0	0
Medicare (US)	31 (14.8)	31 (32.6)	0	0	0	0	0	0
Medicaid (US)	2 (1.0)	2 (2.1)	0	0	0	0	0	0
None (uninsured) (US)	0	0	0	0	0	0	0	0
ECOG PS score, n (%)								
Score 0, fully active	38 (18.1)	20 (21.1)	7 (29.2)	2 (7.7)	5 (20.0)	3 (27.3)	1 (11.1)	0
Score 1	106 (50.5)	44 (46.3)	10 (41.7)	20 (76.9)	10 (40.0)	8 (72.7)	5 (55.6)	9 (45.0)
Score 2	48 (22.9)	22 (23.2)	6 (25.0)	3 (11.5)	8 (32.0)	0	1 (11.1)	8 (40.0)
Score 3	18 (8.6)	9 (9.5)	1 (4.2)	1 (3.9)	2 (8.0)	0	2 (22.2)	3 (15.0)
Score 4, completely disabled	0	0	0	0	0	0	0	0
Time since diagnosis, months								
Mean (SD)	38.7 (44.9)	29.6 (26.3)	54.9 (52.1)	40.9 (50.4)	33.8 (17.9)	44.7 (24.1)	122.9 (90.6)	25.0 (59.9)
Median (IQR)	23 (12–45)	21 (9–40)	37 (18–78)	18 (15–44)	32 (18–42)	36 (32–42)	115 (32–189)	10 (1–19)
Currently receiving treatment, n (%)	97 (46.2)	36 (37.9)	8 (33.3)	17 (65.4)	18 (72.0)	8 (72.7)	9 (100)	1 (5.0)
Current treatment duration, n (%)								
1–2 months	16 (16.5)	6 (16.7)	1 (12.5)	1 (5.9)	6 (33.3)	0	2 (22.2)	0
3–6 months	30 (30.9)	13 (36.1)	3 (37.5)	1 (5.9)	6 (33.3)	5 (62.5)	1 (11.1)	1 (100)
7–12 months	26 (26.8)	13 (36.1)	2 (25.0)	5 (29.4)	1 (5.6)	3 (37.5)	2 (22.2)	0
≥ 1 year	25 (25.8)	4 (11.1)	2 (25.0)	10 (58.8)	5 (27.8)	0	4 (44.4)	0
Transplant eligibility, n (%)								
Transplant eligible	62 (29.5)	25 (26.3)	8 (33.3)	9 (34.6)	10 (40.0)	5 (45.5)	4 (44.4)	1 (5.0)
Transplant experienced	34 (16.2)	16 (16.8)	2 (8.3)	6 (23.1)	4 (16.0)	2 (18.2)	1 (11.1)	3 (15.0)
Transplant ineligible	114 (54.3)	54 (56.8)	14 (58.3)	11 (42.3)	11 (44.0)	4 (36.4)	4 (44.4)	16 (80.0)
Treatment line, n (%)								
2L	148 (70.8)	65 (68.4)	17 (70.8)	18 (69.2)	18 (72.0)	10 (100.0)	3 (33.3)	17 (85.0)
3L+	61 (29.2)	30 (31.6)	7 (29.2)	8 (30.8)	7 (28.0)	0	6 (66.7)	3 (15.0)
Distance to treating hospital, n (%)								
< 50 miles	176 (83.8)	77 (81.1)	18 (75.0)	22 (84.6)	22 (88.0)	10 (90.9)	8 (88.9)	19 (95.0)
≥ 50 miles	34 (16.2)	18 (19.0)	6 (25.0)	4 (15.4)	3 (12.0)	1 (9.1)	1 (11.1)	1 (5.0)

[a]Private insurance included employer-provided insurance, self-provided insurance, personal private insurance, and employer provided private insurance.
ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; SD, standard deviation.

- A total of 210 patients with R/R LBCL across France (n = 9), Germany (n = 25), Italy (n = 26), Japan (n = 20), Spain (n = 11), the UK (n = 24), and the US (n = 95) completed the online survey (**Table 2**)
- The mean age of patients across all countries was 58.8 years. Overall, the majority of respondents were male (n = 112 [53.3%])
- Racial background was collected in the US and UK; approximately one-third (35.3% [n = 60]) of all patients were White, and 21.2% (n = 36) were Black or African American
- The mean time since LBCL diagnosis was 38.7 months before survey completion
- Approximately half of participants (46.2% [n = 97]) were receiving treatment for lymphoma at the time of participation and 53.8% (n = 113) were not
- Of the patients taking treatments at the time of completing the survey, 87.0% (n = 86) of patients were taking a combination of 1–3 treatments and 10.3% (n = 10) were receiving a combination of ≥ 4 (n = 1 missing response). More than half of patients were classified as being transplant ineligible 54.3% (n = 114), 29.5% (n = 62) were transplant eligible, and 16.2% (n = 34) were transplant experienced
- Among participants who reported their treatment duration, 30.9% (n = 30) had treatment lasting 3–6 months, 26.8% (n = 26) had treatment lasting 7–12 months, 25.8% (n = 25) had treatment lasting ≥ 1 year, and 16.5% (n = 16) had treatment lasting 1–2 months

Model selection

- A hurdle latent class logit (HLCL) model was used to account for differences in choice behavior. Preference weights were used to calculate relative attribute importance (RAI) and attribute trade-offs for each class

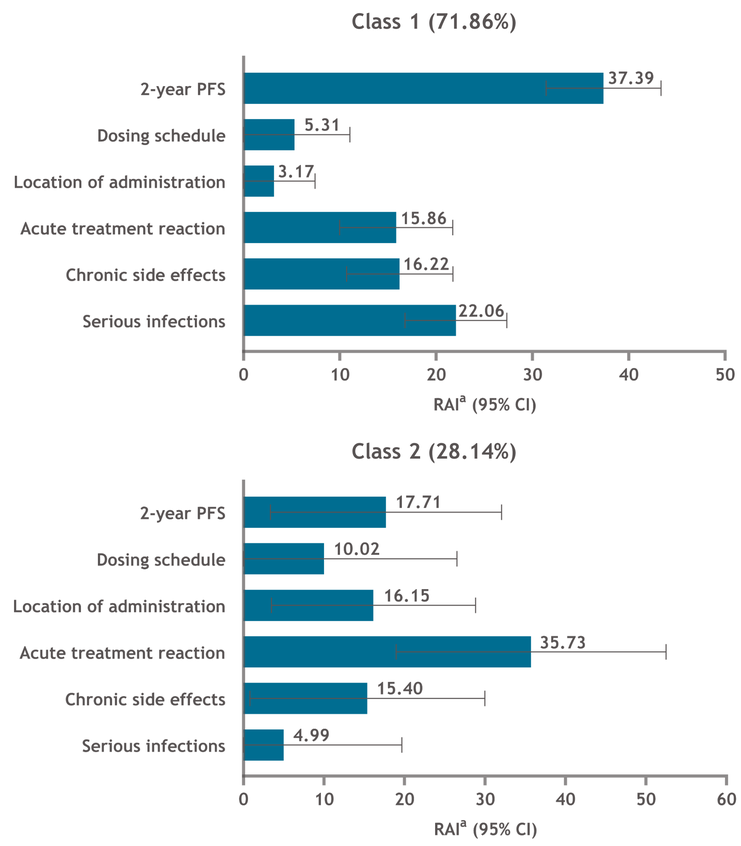
Table 3. HLCL model: marginal utilities

Attributes	Class 1 (71.86%)		Class 2 (28.14%)	
	Marginal utility (SE)	95% CI	Marginal utility (SE)	95% CI
Alternative specific constant				
Treatment A	Reference	–	Reference	–
Treatment B	−0.18 (0.09)[a]	−0.35, −0.02	0.18 (0.12)	−0.06, 0.42
Treatment C	−0.45 (0.20)[a]	−0.83, −0.07	0.74 (0.27)[b]	0.21, 1.26
2-year PFS				
5%	Reference	–	Reference	–
25%	0.79 (0.11)[c]	0.58, 1.00	0.19 (0.16)	−0.11, 0.49
45%	1.39 (0.13)[c]	1.15, 1.64	−0.14 (0.16)	−0.45, 0.18
Dosing schedule				
Multicycle treatment, continuous	Reference	–	Reference	–
Single-cycle treatment	0.20 (0.12)	−0.03, 0.43	0.05 (0.15)	−0.24, 0.35
Multicycle treatment for 6 months	0.20 (0.11)	−0.02, 0.42	0.18 (0.16)	−0.13, 0.50
Location of administration				
Nonlocal hospital	Reference	–	Reference	–
Local hospital	−0.12 (0.08)	−0.28, 0.05	0.30 (0.12)[a]	0.05, 0.54
Acute treatment reaction				
35%	Reference	–	Reference	–
15%	0.35 (0.10)[c]	0.15, 0.55	0.39 (0.15)[a]	0.09, 0.68
0%	0.59 (0.12)[c]	0.36, 0.82	0.66 (0.17)[c]	0.33, 0.99
Chronic side effects				
Moderate	Reference	–	Reference	–
Mild	0.60 (0.12)[c]	0.37, 0.84	−0.15 (0.16)	−0.47; 0.16
None	0.58 (0.13)[c]	0.34, 0.83	0.13 (0.17)	−0.20; 0.46
Serious infections				
30%	Reference	–	Reference	–
10%	0.43 (0.11)[c]	0.21, 0.64	0.08 (0.16)	−0.23, 0.39
0%	0.82 (0.12)[c]	0.58, 1.07	−0.01 (0.16)	−0.33, 0.30

[a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$.
CI, confidence interval; SE, standard error.

- The final analysis identified 2 patterns of choice behavior among patients (**Table 3**)
  - Within Class 1, parameters for 2-year PFS, acute treatment reaction, chronic side effects, and serious infections all had a statistically significant impact on preferences, indicating that patients considered these attributes in their decision-making
  - Within Class 2, ≥ 1 parameter was statistically significant for the acute treatment reaction and location of administration attributes, indicating that in this class, patients considered only a subset of treatment attributes in their decision-making
- Among patients in Class 1, the most important driver of preferences was 2-year PFS followed by the risk of serious infections, chronic side effects, and acute treatment reaction
- Among patients in Class 2, the most important driver of preference was acute treatment reaction, followed by 2-year PFS, location of administration, and chronic side effects
- The probability of belonging to Class 1 or Class 2 was not influenced by sociodemographic and clinical characteristics collected and included in the analysis, suggesting that differences in choice behavior and preferences may be idiosyncratic rather than varying systematically across patient groups
- The trade-offs that patients were willing to make between treatment attributes differed across classes
  - Patients in Class 1 valued an increase in 2-year PFS from 5% to 45% as equivalent to a 79.3% reduction in the risk of acute treatment reaction
  - Patients in Class 2 valued a treatment being administered in a local over nonlocal hospital as equivalent to an 18.2% reduction in the risk of acute treatment reaction
- Patients in Class 1 were more likely to opt into profiles aligned with CAR T cell therapy, while those in Class 2 were more likely to prefer the SOC profile

Figure 2. HLCL model: RAI



[a]A higher RAI score indicates that the attribute is a larger driver of preferences or is more important/influential in patients' treatment decision-making (the lower bounds of the 95% CI was clipped at 0 to improve visibility).

- Efficacy was the most important attribute from Class 1 and acute treatment reaction was the most important for Class 2 (**Figure 2**)

Discussion

- Our results highlight the value of shared patient-clinician decision-making
- The majority of patients' preferences were driven by efficacy and most patients who engaged in making trade-offs were willing to accept large increases in the risks of CAR T cell therapy in exchange for improved efficacy
- A small proportion of patients are likely to be CAR T cell therapy averse, motivated largely by the avoidance of risks associated with this treatment, including cytokine release syndrome and neurologic events
  - Some patients were unwilling to make any trade-offs between treatment attributes and made choices based only on survival outcomes
- Since these patterns of behavior where not clearly linked to observed characteristics, these idiosyncratic preference patterns should be carefully explored by clinicians when developing treatment plans to ensure that patients are being prescribed therapies most in line with their priorities

Conclusions

- Among patients with R/R LBCL, 2 types of choice behavior were identified. CAR T cell therapy adopters preferred hypothetical treatment profiles representing CAR T cell therapy and were willing to accept large increases in the risk of acute treatment reaction to gain improvements in 2-year PFS
- A smaller proportion of patients are CAR T cell therapy averse; these patients preferred to receive a treatment aligned with SOC, and decision-making was driven by avoiding the risk of acute treatment reactions commonly associated with CAR T cell therapy
- The heterogeneity in patient preferences highlights the need for shared patient-clinician decision-making

References

1. American Cancer Society. Types of B-cell lymphoma. https://www.cancer.org/cancer/non-hodgkin-lymphoma/about/b-cell-lymphoma.html. Updated January 29, 2019. Accessed October 11, 2023.
2. Tilly H, et al. *Ann Oncol* 2015;26(suppl 5):v116–v125.
3. Chihara D, et al. *Br J Haematol* 2014;164:536–545.
4. de Bekker-Grob EW, et al. *Patient* 2015;8:373–384.
5. Johnson FR, et al. *Value Health* 2013;16:3–13.

Acknowledgments

- This study was funded by Bristol Myers Squibb
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Emily Burke, PhD, and Jeremy Henriques, PhD, CMPP, of The Lockwood Group (Stamford, CT, USA), funded by Bristol Myers Squibb

Presented at the International Society for Pharmacoeconomics and Outcomes Research Europe (ISPOR EU) Annual Meeting; November 12–15, 2023; Copenhagen, Denmark