Treatment preferences among patients with relapsed/refractory diffuse large B-cell lymphoma in the United States

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

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

Introduction

- Chimeric antigen receptor (CAR) T cell therapy is a treatment option proven to be effective in trials and real-world clinical settings among patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL)[1–5]
- The United States (US) Food and Drug Administration has approved the following 3 such therapies for R/R DLBCL: lisocabtagene maraleucel, axicabtagene ciloleucel, and tisagenlecleucel[6–8]
- Limited quantitative data are available on patients' preferences of CAR T cell therapy attributes for the treatment of R/R DLBCL; here, we report results from the US population from a multicountry preference study

Objective

- To understand how patients with R/R DLBCL value benefits and risks associated with CAR T cell therapy

Methods

- An online best-best discrete choice experiment (BB-DCE) survey was developed using insights from a targeted literature review and available clinical data
- Patients with a self-reported diagnosis of autologous stem cell transplantation—eligible and —ineligible R/R DLBCL were eligible to participate in the survey
- The full survey was pilot tested with 20 patients; 95 US patients completed the final survey
- The BB-DCE included 9 experimentally designed choice tasks consisting of 3 hypothetical treatment profiles, including a fixed profile representing standard of care (non—CAR T)
- An example choice task is shown in **Figure 1**
- The BB-DCE included the following 6 attributes: treatment success, treatment intake and dosing schedule, location of administration, risk of acute treatment reaction, risk of serious infections, and chronic side effects while on treatment (**Table 1**)
- A mixed logit model estimated preference weights, which were used to calculate relative attribute importance (RAI) and quantify attribute trade-offs as marginal rates of substitution (MRS). Standard errors and 95% confidence intervals (CI) for MRS were estimated using the Delta method

Figure 1. BB-DCE example choice task

Attribute	Treatment A	Treatment B	Treatment C[a]
Treatment success	25 out of 100 (25%)	5 out of 100 (5%)	5 out of 100 (5%)
Dosing schedule	Single-cycle treatment	Multicycle treatment for 6 months	Multicycle treatment, continuous until disease progression
Location of administration	Nonlocal hospital	Local hospital	Local hospital
Risk of acute treatment reaction	35 out of 100 (35%)	15 out of 100 (15%)	0 out of 100 (0%)
Chronic side effects while on treatment	Mild	Mild	Moderate
Risk of experiencing serious infections	10 out of 100 (10%)	0 out of 100 (0%)	30 out of 100 (30%)
Which treatment would be your first choice?	☐	☐	☐
Of the remaining 2 alternatives, which treatment would be your preferred choice?	☐	☐	☐

[a]Treatment C was the fixed profile across all tasks and always included the levels as shown in this example.

Table 1. BB-DCE attributes and levels

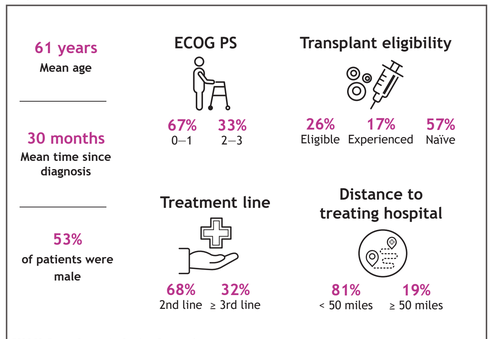
Attributes	Definition	Levels
Treatment success	The chance of surviving and being in remission 2 years after starting treatment. How well treatments work is measured by how well the cancer responds to treatment. A good response usually means patients will survive longer and achieve remission (ie, they no longer experience cancer symptoms or require treatment).	1. 5 out of 100 patients (5%) 2. 25 out of 100 patients (25%) 3. 45 out of 100 patients (45%)
Treatment intake and 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 and can be life-threatening. Symptoms include high fever, fatigue, nausea, organ failure, confusion, headaches, and seizures.	1. 0 out of 100 patients (0%) 2. 15 out of 100 patients (15%) 3. 35 out of 100 patients (35%)
Chronic side effects while on treatment	The severity of chronic side effects 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 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, which 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 patients (0%) 2. 10 out of 100 patients (10%) 3. 30 out of 100 patients (30%)

Results

Patients

- Among 95 patients enrolled in the survey, mean age was 61 years and 53% were male
- Forty-three percent of patients were eligible for stem cell transplantation (self-reported) or had received one, and 68% were receiving second-line treatment at the time of the survey
- Full sample characteristics are shown in **Figure 2**

Figure 2. Sample characteristics

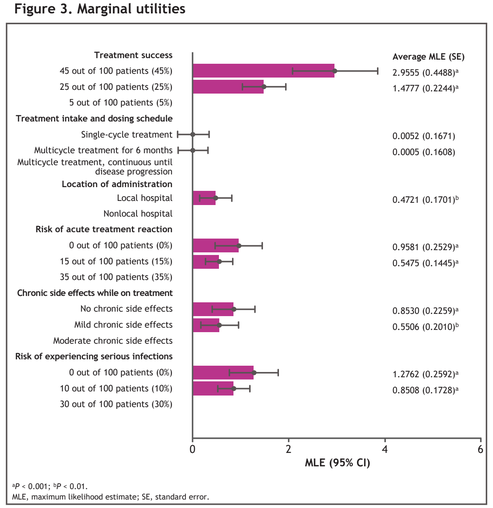


ECOG PS, Eastern Cooperative Oncology Group performance status.

Treatment preferences: marginal utilities

- Patients preferred treatments with lower levels of risk and higher levels of treatment benefit or convenience (location of administration) (**Figure 3**)
- With the exception of treatment intake and dosing schedule, all attributes had a statistically significant impact on treatment preferences

Figure 3. Marginal utilities

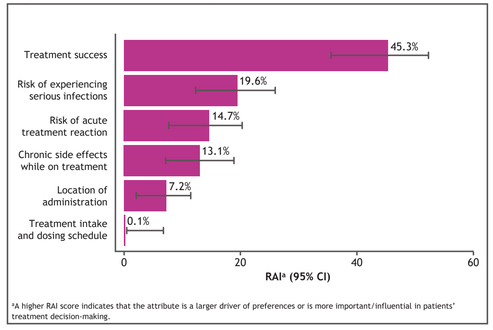


[a]$P < 0.001$; [b]$P < 0.01$.
MLE, maximum likelihood estimate; SE, standard error.

Treatment preferences: relative attribute importance

- Probability of treatment success had the largest influence on treatment preferences (RAI 45.3%), followed by risk of serious infections (RAI 19.6%) and acute treatment reactions (RAI 14.7%). Chronic side effects (RAI 13.1%), location of administration (RAI 7.2%), and dosing schedule (RAI 0.1%) were less influential on patients' treatment decision-making (**Figure 4**)
- Based on the RAI scores, treatment success was 2.3 times more important than the risk of serious infections, and 3.1 times more important than the risk of acute treatment reaction
- The importance patients placed on the risk of experiencing serious infections differed based on living status; patients who lived with others cared more about this risk (RAI 21.5%) than those who lived alone (RAI 2.2%) ($P < 0.05$)

Figure 4. Relative attribute importance



[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.

Marginal rates of substitution: treatment success

- To reduce the risk of acute treatment reaction from 35% to 0%, patients would be willing to accept a 12.97% decrease in the chance of treatment success (**Table 2**)
- To reduce the risk of experiencing serious infections from 30% to 10%, patients would be willing to accept a 11.51% decrease in the chance of treatment success
- Having treatment available in a local hospital was valued as being equivalent to a 6.39% chance to treatment success

Table 2. Marginal rates of substitution: treatment success

Attribute	Level	MRS (SE)	95% CI
Treatment intake and dosing schedule	Multicycle treatment, continuous until disease progression	REFERENCE	
	Multicycle treatment for 6 months	0.01% (2.18)	−4.26—4.27
	Single-cycle treatment	0.07% (2.26)	−4.37—4.51
Location of administration	Nonlocal hospital	REFERENCE	
	Local hospital	6.39% (2.30)	1.87—10.91
Risk of acute treatment reaction	35%	REFERENCE	
	15%	7.41% (1.99)	3.51—11.31
	0%	12.97% (3.48)	6.14—19.79
Chronic side effects while on treatment	Moderate chronic side effects	REFERENCE	
	Mild chronic side effects	7.45% (2.85)	1.86—13.04
	No chronic side effects	11.54% (3.30)	5.08—18.01
Risk of experiencing serious infections	30%	REFERENCE	
	10%	11.51% (2.64)	6.34—16.69
	0%	17.27% (3.96)	9.52—25.03

Marginal rates of substitution: risk of serious infections

- A change in the risk of acute treatment reaction from 35% to 0% was valued as being equivalent to a 22.52% risk of serious infections (**Table 3**)
- A change in the risk of chronic side effects while on treatment from moderate to mild was valued as being equivalent to a 12.94% risk of serious infections
- Having treatment available in a local hospital was valued as being equivalent to a 11.10% risk of serious infections

Table 3. Marginal rates of substitution: risk of serious infections

Attribute	Level	MRS (SE)	95% CI
Treatment success	5%	REFERENCE	
	25%	34.74% (7.96)	19.14—50.34
	45%	69.48% (15.92)	38.28—100.67
Treatment intake and dosing schedule	Multicycle treatment, continuous until disease progression	REFERENCE	
	Multicycle treatment for 6 months	0.01% (3.78)	−7.40—7.42
	Single-cycle treatment	0.12% (3.93)	−7.58—7.82
Location of administration	Nonlocal hospital	REFERENCE	
	Local hospital	11.10% (4.51)	2.26—19.94
Risk of acute treatment reaction	35%	REFERENCE	
	15%	12.87% (3.87)	5.28—20.46
	0%	22.52% (6.78)	9.24—35.80
Chronic side effects while on treatment	Moderate chronic side effects	REFERENCE	
	Mild chronic side effects	12.94% (5.72)	1.73—24.16
	No chronic side effects	20.05% (6.84)	6.65—33.45

Conclusions

- A key driver of patients' preferences in choice of treatment for R/R DLBCL was treatment success, which was more than 2 times as important as the risk of experiencing serious infections, and more than 3 times as important as the risk of acute treatment reaction
- Patients were willing to make trade-offs between treatment risks and benefits and valued a treatment that could be offered at a local hospital over a treatment that would require travel to a nonlocal hospital
- The BB-DCE survey is also being fielded in the United Kingdom, Germany, Italy, Spain, France, and Japan; results will be reported elsewhere

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Email: FeiFei.Liu@bms.com