

# Rituximab/Bendamustine or Rituximab/Ifosfamide/Carboplatin/Etoposide as Second-Line Therapy for Relapsed/Refractory Diffuse Large B-Cell Lymphoma: A Real-World Analysis

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## Research Article

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# Abstract

Rituximab/bendamustine (RB) and rituximab/ifosfamide/carboplatin/etoposide (R-ICE) are commonly used to treat relapsed/refractory diffuse large B-cell lymphoma (DLBCL), although their effectiveness has not been compared in real-world practice. This study evaluated data from DLBCL patients who relapsed after or were refractory to first-line therapy in an electronic health record (EHR)-derived database between 2011 and 2018. One hundred thirty-seven patients using RB and 270 patients using R-ICE were included for analysis. Transplantation after second-line therapy was considered a censored event in the time-to-event analyses. Patients in the RB group were older and had poorer performance status while there were no significant differences in stage, cell of origin, and double-/triple-hit subtypes. Relative to the R-ICE group, the RB group had significantly longer time-to-next-treatment (TTNT) and overall survival (OS). Subgroup analyses revealed that patients who were <70 years or had better performance status consistently had better TTNT and OS if they had received RB. Patients who had disease progression within 12 months after induction chemotherapy had a significantly inferior prognosis, regardless of the salvage treatments. Multivariable analysis revealed that RB treatment independently predicted better TTNT and OS. These data indicate that RB may be an alternative to R-ICE as second-line therapy for selected DLBCL patients.

## Introduction

During the last two decades, the development of combination immunochemotherapeutic regimens that incorporate rituximab (an anti-CD20 monoclonal antibody) has improved the response rates to induction therapy among patients with diffuse large B-cell lymphoma (DLBCL). Although R-CHOP treatment (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) initially achieves complete response (CR) in 70–80% of patients, 20% of patients have primary refractory disease and another 20–30% of patients eventually experience disease recurrence.<sup>1–6</sup> Thus, salvage therapies are needed to improve survival outcomes.<sup>7–12</sup>

The CORAL study evaluated 191 patients who received second-line R-ICE therapy (rituximab, ifosfamide, etoposide, and carboplatin) and revealed a response rate of 64%, with 3-year rates of 31% for progression-free survival (PFS) and 47% for overall survival (OS).<sup>9</sup> However, only 51% of the patients in the study underwent autologous stem cell transplantation (ASCT), which was primarily related to an insufficient response to the second-line treatment. Treatment using rituximab plus bendamustine (RB) is a popular alternative for patients who are not eligible for intensive treatment because of advanced age or comorbidities.<sup>13–15</sup> Various studies have revealed response rates of approximately 40–60% to RB treatment among patients with relapsed/refractory DLBCL, including among patients who were 5–10 years older than the patients in the CORAL study.<sup>16–19</sup>

However, to the best of our knowledge, no studies have compared the effectiveness of RB and R-ICE as second-line treatments for relapsed/refractory DLBCL. Therefore, this study involved a real-world analysis

to evaluate the effectiveness of these regimens, as well as the clinical parameters that might influence the long-term survival outcomes.

## Results

The Flatiron Health database included records for 5,787 patients who were diagnosed with DLBCL during 2011–2018, including 5,356 patients (92.6%) who received induction chemotherapy for DLBCL. The most commonly used regimens were R-CHOP-like regimens (78%, Table S1). Among patients who received induction therapy, 135 patients (2.5%) underwent upfront SCT after induction chemotherapy, 1,365 patients (25.5%) underwent second-line treatment for DLBCL, 2,888 patients (53.9%) did not receive further treatment until the data lock date (December 31, 2019), and 968 patients (18.1%) died during or after induction therapy. Therefore, the final study population included 137 patients in the RB group and 270 patients in the R-ICE group (Figure 1). The most commonly used second-line treatments were the RB and R-ICE regimens (Table S2).

## Comparing the clinical characteristics of patients who received RB or R-ICE treatment

Table 1 shows that patients in the RB group were older than patients in the R-ICE group (median age: 77 years *vs.* 60 years). The RB group was also more likely to have an ECOG performance status of 2–3 and less likely to have received R-CHOP-like regimens as induction therapy. There were no significant differences in terms of sex, race, calendar year of diagnosis, stage at diagnosis, cell of origin (GCB *vs.* non-GCB), Ki-67 index, proportion of the double-/triple-hit subtypes, number of extranodal sites, rwPOD, or the time from the end of induction therapy to the start of second-line treatment.

## Analyses of TTNT and OS

Relative to the R-ICE group, the group that received second-line RB had significantly longer median TTNT (5.7 months *vs.* 9.2 months, aHR: 1.448, 95% CI: 1.04–2.01,  $p=0.0276$ ) and significantly longer median OS (9.2 months *vs.* 15.9 months, aHR: 1.589, 95% CI: 1.116–2.263,  $p=0.0102$ ) (Figure 2). Subgroup analyses revealed that, relative to patients with rwPOD at >12 months and regardless of the second-line treatment, patients with rwPOD at  $\leq 12$  months had significantly shorter median TTNT (16.1 months *vs.* 4.6 months, aHR: 1.925, 95% CI: 1.442–2.568,  $p<0.0001$ ) and significantly shorter median OS (26.8 months *vs.* 8.5 months, aHR: 1.863, 95% CI: 1.348–2.574,  $p=0.0002$ ) (Figure 3). However, among patients with rwPOD at >12 months and relative to the RB subgroup, the R-ICE subgroup had significantly shorter median TTNT (21.3 months *vs.* 9.6 months, aHR: 2.429, 95% CI: 1.341–4.399,  $p=0.0034$ ) and significantly shorter median OS (26.9 months *vs.* 22.8 months, aHR: 2.446, 95% CI: 1.226–4.883,  $p=0.0112$ ) (Figure 3). Furthermore, among patients who were <70 years old and relative to the R-ICE subgroup, the RB subgroup had significantly longer TTNT and OS, while there was no significant difference between the RB and R-ICE subgroups among patients who were  $\geq 70$  years old (Figure S1). Among patients with an ECOG performance status of 0–1 and relative to the R-ICE subgroup, the RB subgroup had longer TTNT and OS,

while there was no significant difference between the RB and R-ICE subgroups among patients with an ECOG performance status of 2–3 (Figure S2).

The multivariable analysis revealed that, relative to RB treatment, R-ICE treatment was independently associated with poorer TTNT (aHR: 1.448,  $p=0.028$ ) and poorer OS (aHR: 1.589,  $p=0.01$ ) (Table 2). Relative to rwPOD at  $\leq 12$  months, rwPOD at  $>12$  months was independently associated with better TTNT (aHR: 0.520,  $p<0.0001$ ) and better OS (aHR: 0.537,  $p=0.0002$ ) (Table 2). Moreover, in the RB subgroup, significantly shorter TTNT and OS outcomes were associated with older age and rwPOD at  $\leq 12$  months (Table S3). In the R-ICE subgroup, only rwPOD at  $\leq 12$  months predicted shorter TTNT, while older age and rwPOD at  $\leq 12$  months both predicted shorter OS (Table S4).

Table 2

Multivariable analyses of time to next treatment and overall survival among 407 DLBCL patients who received RB or R-ICE as second-line treatment

		Time to next treatment			Overall survival		
Parameter		Hazard ratio	95% confidence interval	P-value	Hazard ratio	95% confidence interval	P-value
Treatment (ref: RB)	R-ICE	1.448	1.042–2.013	0.0276	1.589	1.116–2.263	0.0102
Age at second-line treatment		1.004	0.991–1.016	0.5635	1.024	1.009–1.039	0.0014
Time from diagnosis to the start of second-line treatment (ref: ≤12 months)	>12 months	0.520	0.389–0.693	<0.0001	0.537	0.388–0.742	0.0002
ECOG performance status (ref: 0–1)	2–3	1.156	0.757–1.764	0.5027	1.125	0.711–1.779	0.6144
Stage at diagnosis (ref: I–II)	III	1.170	0.769–1.781	0.4628	1.412	0.877–2.275	0.1556
	IV	0.919	0.601–1.404	0.6954	1.287	0.798–2.076	0.3004
Major lymphoma-related genetic changes (ref: MYC–/both BCL–)	Double-/triple-hit	1.108	0.663–1.854	0.6952	1.224	0.707–2.119	0.4704
Number of extranodal sites (ref: 0)	1	0.972	0.716–1.319	0.8556	0.980	0.694–1.384	0.9094
	≥2	1.447	0.919–2.278	0.1109	1.193	0.720–1.977	0.4934

DLBCL: diffuse large B-cell lymphoma, RB: rituximab/bendamustine, R-ICE: rituximab/ifosfamide/carboplatin/etoposide, ECOG: Eastern Cooperative Oncology Group.

## Discussion

Previous studies have revealed poor outcomes among patients with relapsed/refractory DLBCL,<sup>1,2,6</sup> although there is no consensus regarding the optimal second-line treatment at this time.<sup>9-12, 17,19-21</sup> To the best of our knowledge, this is the first study to compare RB and R-ICE as second-line treatments for relapsed/refractory DLBCL. The de-identified EHR-derived database was used to perform real-world analysis of patients who were treated outside of clinical trials, which revealed that the RB group had significantly longer TTNT and OS than the R-ICE group, despite patients in the RB group tending to be older and have poorer ECOG performance statuses. The multivariable analysis revealed that second-line RB treatment appeared to reduce the risk of relapse or death, regardless of age, rwPOD, ECOG performance status, stage at diagnosis, double-/triple-hit subtype, and number of extranodal sites.

The CORAL study and other studies of non-Hodgkin lymphoma revealed that early progression predicted poor OS, without any significant differences in the effects of the second-line regimens.<sup>9,22-24</sup> In the present study, the median time from diagnosis to the start of second-line treatment (which we interpreted as rwPOD) was  $\leq 12$  months for the RB and R-ICE groups, which reflects the aggressive nature of relapsed/refractory DLBCL. As expected, patients in our study with rwPOD at  $\leq 12$  months had poorer outcomes than patients with rwPOD at  $>12$  months, and patients with early relapse did not exhibit any treatment-specific differences in their TTNT and OS outcomes.

The treatment outcomes varied between the RB and R-ICE groups, as death was observed for 91 patients in the RB group (66%) and 103 patients in the R-ICE group (39%). Furthermore, ASCT was only performed for two patients in the RB group (1.5%), while ASCT was performed for 124 patients in the R-ICE group (46%). These differences reflect real-world practice, where younger and more fit patients tend to receive R-ICE treatment, while more frail patients tend to receive RB treatment. Nevertheless,  $>50\%$  of the patients in the R-ICE group experienced second-line treatment failure and were not able to undergo ASCT, which highlights the difficulty in identifying patients who can ultimately undergo ASCT after intensive chemotherapy.

The multicenter phase III CORAL study established the utility of R-ICE treatment, although there have been no significant subsequent improvements in salvage therapies for relapsed/refractory DLBCL.<sup>9</sup> Only approximately 30–50% of these patients respond to intensive second-line chemotherapy and can undergo transplantation.<sup>10</sup> Furthermore, the 3-year PFS rates were 37% in the CORAL study and 28% in the LY.12 study, while the 2-year PFS rate was 25% in the ORCHARRD Study.<sup>9-11</sup>

Ohmachi *et al.*'s multicenter phase II study revealed an overall response rate (ORR) of 63% to RB treatment, and  $>60\%$  of those patients were  $\geq 65$  years old and 57/59 patients had previously received rituximab-containing regimens.<sup>17</sup> Although the median PFS was relatively short, it is noteworthy that the patient population was also relatively frail. Merchionnea *et al.* performed a retrospective real-world analysis and reported an ORR of 50% and a median PFS of eight months among 28 patients who received RB for relapsed/refractory DLBCL.<sup>18</sup> Another multicenter study revealed an ORR of 55% for RB treatment among 58 patients with relapsed/refractory DLBCL, and 60% of those patients had previously received treatment using R-ICE, R-ESHAP (etoposide, methylprednisolone, high-dose cytarabine, cisplatin), R-DHAP

(dexamethasone, high-dose cytarabine, cisplatin), or R-GDP (gemcitabine, dexamethasone, cisplatin).<sup>25</sup> These results highlight the need for better therapeutic and diagnostic strategies. Unfortunately, despite the majority of patients not responding to even intensive chemotherapies, our understanding of the biomolecular basis for chemoresistance in relapsed/refractory DLBCL remains limited. Furthermore, there are few prognostic biomarkers that can be used to guide the selection of patients who are likely to respond to intensive chemotherapy and undergo ASCT or patients who are more suitable for alternative or novel treatment options. For example, some early-phase studies have provided promising data regarding the use of targeted therapy in combination regimens for treating relapsed/refractory DLBCL.<sup>26-33</sup> Nevertheless, long-term follow-up data are needed to evaluate the real-world outcomes of targeted therapy in this setting.

This study provided real-world results regarding second-line treatments for patients with relapsed/refractory DLBCL. However, the retrospective design is subject to various confounding factors, and it would be difficult to assess the potential contributions of these factors. In addition, we substituted TTNT for PFS (a more commonly used endpoint), as the EHRs did not contain sufficient data to calculate PFS. Nevertheless, TTNT may be a clinically meaningful endpoint and has become increasingly used in real-world practice.<sup>34-39</sup> Lastly, this study included patients who were treated during a prolonged study period, and changes in treatment strategy may be a relevant factor, although we confirmed that the calendar years of diagnosis were fairly evenly distributed in both groups (Table 1).

In summary, we believe that this is the first real-world analysis to compare the effectiveness of second-line treatment using RB or R-ICE for relapsed/refractory DLBCL. The results suggest that second-line RB treatment is a potential alternative to R-ICE for select patients with DLBCL, such as younger patients with a fair ECOG performance status or POD at >12 months. However, further studies are needed to validate these findings.

## Patients And Methods

### *Clinical data extraction*

This observational study used the Flatiron Health EHR-derived de-identified database, which is a longitudinal, geographically and demographically diverse database that includes de-identified data from >280 cancer clinics (approximately 800 care sites) and >2.4 million American cancer patients.<sup>40</sup> The patient-level data include structured and unstructured data that were collected via technology-enabled chart abstraction, based on physician's notes and other unstructured documents.

### *Ethics approval and consent to participate*

All experimental protocols were approved by the Research Ethic Committee of National Taiwan University Hospital (approval number 202004077W) and with the Helsinki Declaration of 1975, as revised in 2008. The Research Ethic Committee waived the requirement for informed consent.

## ***Patients and treatments***

The EHR data were collected from January 1, 2011 to December 31, 2019, and we evaluated patients who were diagnosed with DLBCL between January 1, 2011 and December 31, 2018. Patients who received RB as second-line treatment for DLBCL were assigned to the “RB group” and patients who received R-ICE were assigned to the “R-ICE group”. The index date was defined as the date the patient started RB or R-ICE treatment. Oncologist-defined and rule-based lines of treatment were considered, although drugs administered within 28 days were generally considered within the same line of treatment, while a subsequent line of treatment was considered when the patient received any additional immunochemotherapy agents or had a treatment gap of >120 days.

## ***Endpoints***

The present study used the time to next treatment (TTNT) and OS as real-world endpoints. The TTNT outcome was used as a surrogate for PFS, as the real-world database did not contain data regarding the timing of disease progression/relapse. The TTNT interval was defined as the time from the index date to the first instance of the next treatment line or death. The OS interval was defined as the time from the index date to the time of death because of any cause. Patients were censored on the dates of receiving autologous or allogeneic stem cell transplantation (SCT), a disease course-modifying therapy, or the last follow-up. The time from diagnosis to the start of second-line treatment was interpreted as a substitute for real-world progression of disease (rwPOD).

## ***Statistical analysis***

Continuous variables were reported as median (range) and were compared using the Mann-Whitney U test. Categorical variables were reported as number (%) and compared using Fisher’s exact test or the  $\chi^2$  test. The categorical variables were defined as Eastern Cooperative Oncology Group (ECOG) performance status, stage at diagnosis, cell of origin (germinal center B-cell [GCB]-like, GCB, or non-GCB),<sup>41-43</sup> Ki-67 index,<sup>44,45</sup> major lymphoma-related genetic changes,<sup>46-49</sup> and number of extranodal sites. The Kaplan-Meier method was used to plot TTNT and survival curves, which were compared using the log-rank test. Survival analyses were also performed using a Cox proportional hazards model, and the results were reported as adjusted hazard ratios (aHRs) with the 95% confidence intervals (CIs). The model was adjusted for clinical prognostic factors, which included age, rwPOD, ECOG performance status, stage at diagnosis, double-/triple-hit subtypes, and the number of extranodal sites. Differences were considered significant at two-sided P-values of <0.05 and all analyses were performed using SAS software (Studio Enterprise version 3.7).

## **Declarations**

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**Authors' contributions:** YHW contributed to the study's conception and design, development of the statistical analysis plan, data interpretation, literature research, and drafting the manuscript. CYS contributed to the study's conception and design, development of the statistical analysis plan, data analysis, and drafting the manuscript. LCC and MY contributed to the study's conception and design, as well as data interpretation. BSK planned, designed, and coordinated the study throughout the entire study period and drafted the manuscript.

**Declarations of interests:** CYS and LCC are employed by Roche Products Ltd., Taiwan. Flatiron Health, Inc. is an independent subsidiary of the Roche Group. YHW, MY, and BSK declare that they have no competing interests.

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**Data availability:** The data that support the findings of this study have been originated by Flatiron Health, Inc. These de-identified data may be made available upon request, and are subject to a license agreement with Flatiron Health; interested researchers should contact <DataAccess@flatiron.com> to determine licensing terms.

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## Tables

**Table I. Clinical and laboratory characteristics of 407 DLBCL patients who received RB or R-ICE as second-line treatment**

	<b>RB (n=137)</b>	<b>R-ICE (n=270)</b>	<b>P value</b>
<b>Male sex, n (%)</b>	71 (51.8)	166 (61.5)	0.0619
<b>Caucasian, n (%)</b>	106 (77.4)	184 (68.2)	0.0520
<b>Calendar year of diagnosis</b>			0.9573
2011–2014	77 (56.2)	151 (55.9)	
2015–2018	60 (43.8)	119 (44.1)	
<b>Age at second-line treatment, years*</b>	77 (40–85)	60 (21–84)	<0.0001
<b>Time from diagnosis to the start of second-line treatment (rwPOD), months*</b>	10.2 (1–64.2)	9.4 (0.5–83.7)	0.1871
<b>Time from the end of induction therapy to the start of second-line treatment, months*</b>	5.3 (0.3–60.1)	4.0 (0.3–64.6)	0.3633
<b>R-CHOP-based regimens as induction therapy, n (%)</b>	104 (75.9)	245 (90.7)	<0.0001
<b>ECOG performance status, n (%)</b>			0.0003
0–1	54 (66.7)	111 (87.4)	
2–3	27 (33.3)	16 (12.6)	
Unknown	56	143	
<b>Stage at diagnosis, n (%)</b>			0.8318
I–II	24 (24.0)	49 (23.4)	
III	34 (34.0)	65 (31.1)	
IV	42 (42.0)	95 (45.5)	
Unknown	37	61	
<b>Cell of origin, n (%)</b>			0.5675
Germinal B-cell	36 (61.0)	77 (56.6)	
Non-germinal B-cell	23 (39.0)	59 (43.4)	
Unknown	78	134	
<b>Ki-67 index, n (%)</b>			>0.999
Low (<30%)	3 (3.9)	6 (3.6)	
High (≥30%)	75 (96.2)	161 (96.4)	
Unknown	59	103	

<b>Major lymphoma-related genetic changes, n (%)</b>	0.2810		
- MYC-/both BCL-	67 (93.1)	170 (88.5)	
- Double-/triple-hit (MYC and BCL2 and/or BCL6)	5 (6.9)	22 (11.5)	
- Unknown	65	78	
<b>Number of extranodal sites, n (%)</b>	0.2532		
0	80 (58.4)	141 (52.2)	
1	45 (32.8)	91 (33.7)	
≥2	12 (8.8)	38 (14.1)	
<b>Extranodal sites, n (%)</b>			
Bone marrow	14 (10.2)	32 (11.9)	0.6230
Bone	11 (8.0)	30 (11.1)	0.3290
Central nervous system	3 (2.2)	5 (1.9)	>0.999
Pulmonary	11 (8.0)	25 (9.3)	0.6796
Liver/gastrointestinal	15 (10.9)	44 (16.3)	0.1476
Renal/adrenal	2 (1.5)	9 (3.3)	0.3475

Data are presented as number (%) or median (range).

DLBCL: diffuse large B-cell lymphoma, RB: rituximab/bendamustine, R-ICE:

rituximab/ifosfamide/carboplatin/etoposide, R-CHOP:

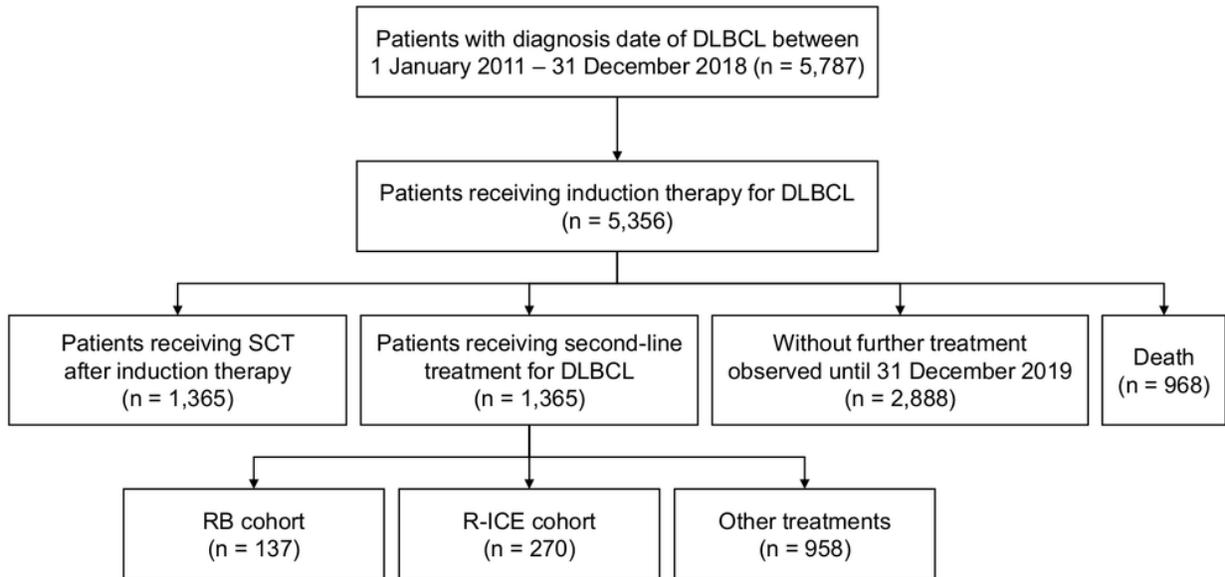
rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone, ECOG: Eastern Cooperative Oncology Group, rwPOD: real-world progression of disease

**Table 2. Multivariable analyses of time to next treatment and overall survival among 407 DLBCL patients who received RB or R-ICE as second-line treatment**

Parameter		Time to next treatment			Overall survival		
		Hazard ratio	95% confidence interval	P-value	Hazard ratio	95% confidence interval	P-value
Treatment (ref: RB)	R-ICE	1.448	1.042–2.013	0.0276	1.589	1.116–2.263	0.0102
Age at second-line treatment		1.004	0.991–1.016	0.5635	1.024	1.009–1.039	0.0014
Time from diagnosis to the start of second-line treatment (ref: ≤12 months)	>12 months	0.520	0.389–0.693	<0.0001	0.537	0.388–0.742	0.0002
ECOG performance status (ref: 0–1)	2–3	1.156	0.757–1.764	0.5027	1.125	0.711–1.779	0.6144
Stage at diagnosis (ref: I–II)	III	1.170	0.769–1.781	0.4628	1.412	0.877–2.275	0.1556
	IV	0.919	0.601–1.404	0.6954	1.287	0.798–2.076	0.3004
Major lymphoma-related genetic changes (ref: MYC–/both BCL–)	Double-/triple-hit	1.108	0.663–1.854	0.6952	1.224	0.707–2.119	0.4704
Number of extranodal sites (ref: 0)	1	0.972	0.716–1.319	0.8556	0.980	0.694–1.384	0.9094
	≥2	1.447	0.919–2.278	0.1109	1.193	0.720–1.977	0.4934

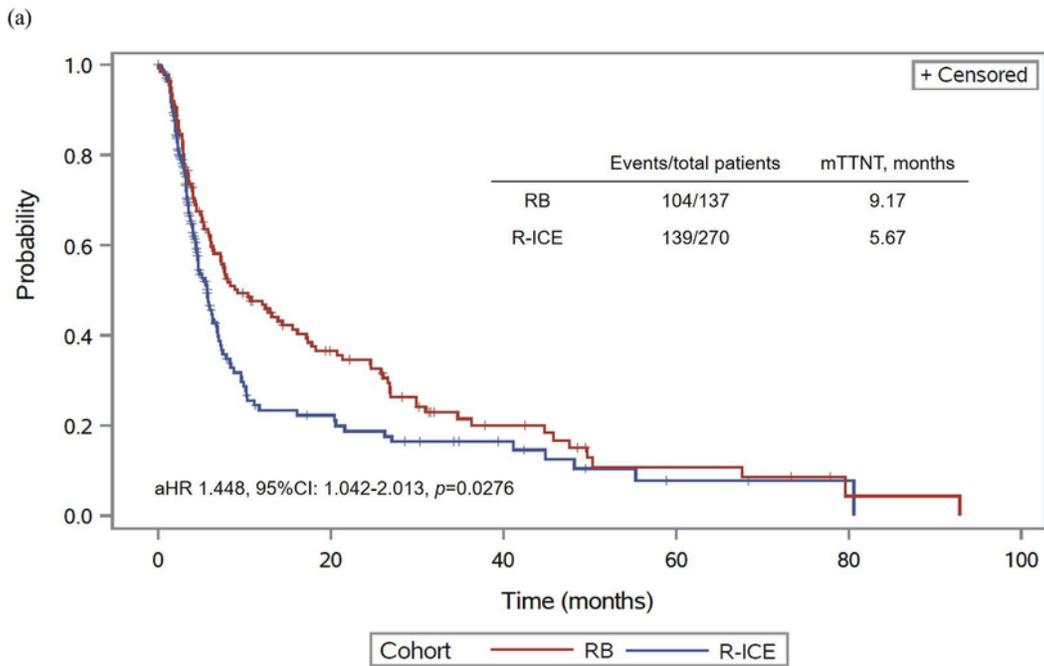
DLBCL: diffuse large B-cell lymphoma, RB: rituximab/bendamustine, R-ICE: rituximab/ifosfamide/carboplatin/etoposide, ECOG: Eastern Cooperative Oncology Group.

## Figures

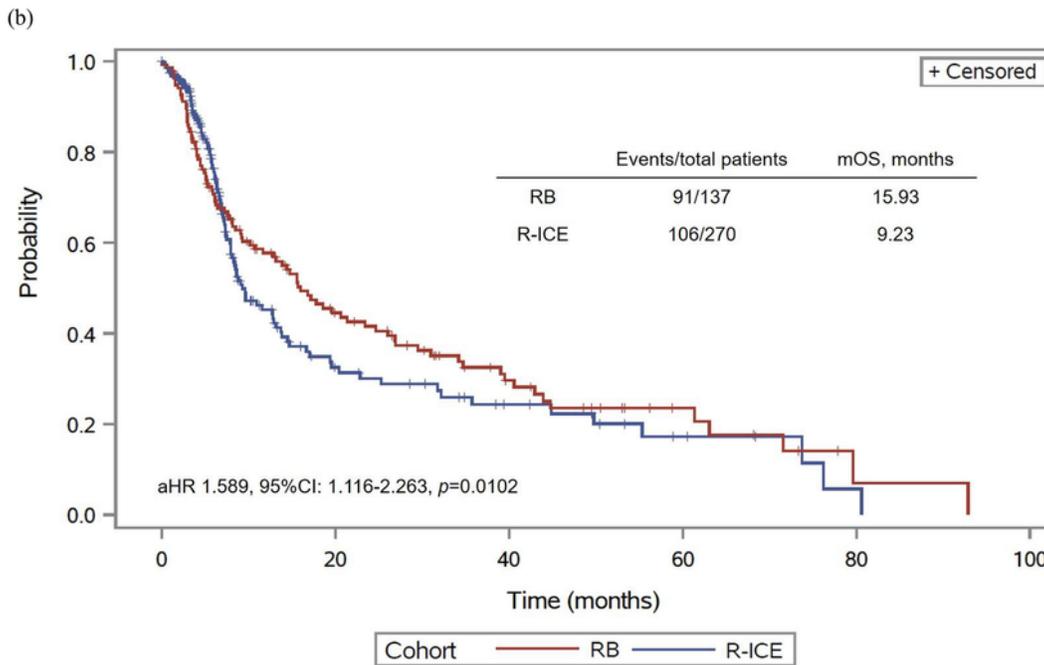


**Figure 1**

Flow chart for patient identification.



RB	137	87	59	45	37	32	22	15	13	11	6	5	5	5	4	3	1	1	1	0
R-ICE	270	64	28	21	19	16	13	10	9	6	4	4	2	2	1	1	1	1	0	

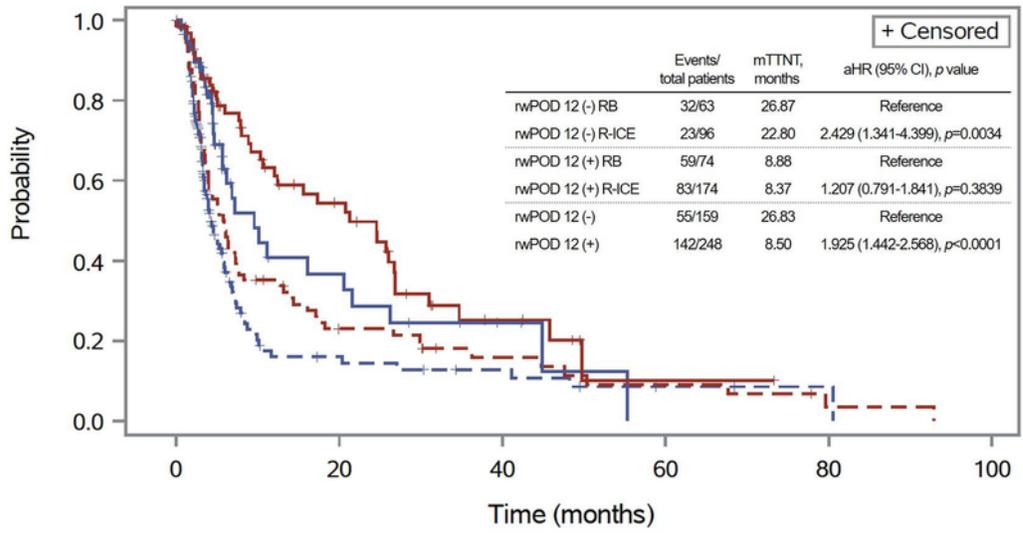


RB	137	98	72	56	45	40	33	24	20	15	13	10	8	6	5	3	1	1	1	0
R-ICE	270	117	53	34	27	24	21	16	13	11	9	7	5	4	3	2	1	1	0	

## Figure 2

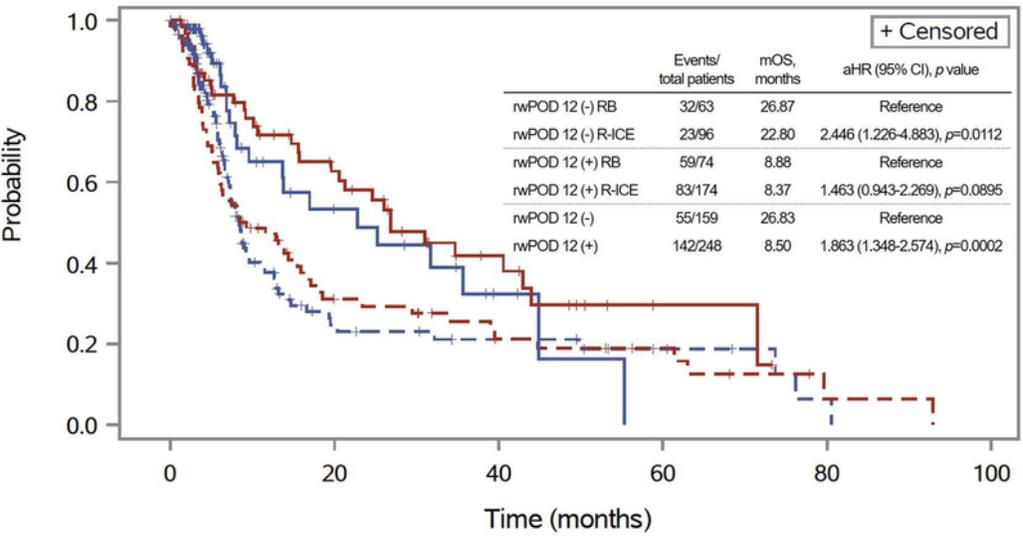
Kaplan-Meier curves for 407 DLBCL patients according to their second-line treatment regimen. Curves are shown for the time to next treatment (TTNT, a) and overall survival (OS, b) among 137 patients who received second-line rituximab/bendamustine (RB) and 270 patients who received second-line rituximab/ifosfamide/carboplatin/etoposide (R-ICE). Patients who received RB had significantly longer TTNT and OS than patients who received R-ICE.

(a)



	rwPOD 12 (-) RB	rwPOD 12 (-) R-ICE	rwPOD 12 (+) RB	rwPOD 12 (+) R-ICE
rwPOD 12 (-) RB	63	46	34	26
rwPOD 12 (-) R-ICE	96	24	13	10
rwPOD 12 (+) RB	74	41	25	19
rwPOD 12 (+) R-ICE	174	40	15	11

(b)



	rwPOD 12 (-) RB	rwPOD 12 (-) R-ICE	rwPOD 12 (+) RB	rwPOD 12 (+) R-ICE
rwPOD 12 (-) RB	63	47	38	31
rwPOD 12 (-) R-ICE	96	36	19	14
rwPOD 12 (+) RB	74	51	34	25
rwPOD 12 (+) R-ICE	174	81	34	20

Figure 3

Kaplan-Meier curves stratified according to real-world progression of disease (rwPOD) and the different regimens. Curves are shown for the time to next treatment (TTNT, a) and overall survival (OS, b) among patients who received the different regimens and patients with real-world progression of disease (rwPOD) at  $\leq 12$  months or  $>12$  months. Patients with rwPOD at  $\leq 12$  months had shorter TTNT and OS than patients with rwPOD at  $>12$  months, regardless of the second-line treatment they received. However,

patients with rwPOD at >12 months had significantly longer TTNT and OS if they received rituximab/bendamustine (RB), relative to the other regimens.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarymaterial.pdf](#)