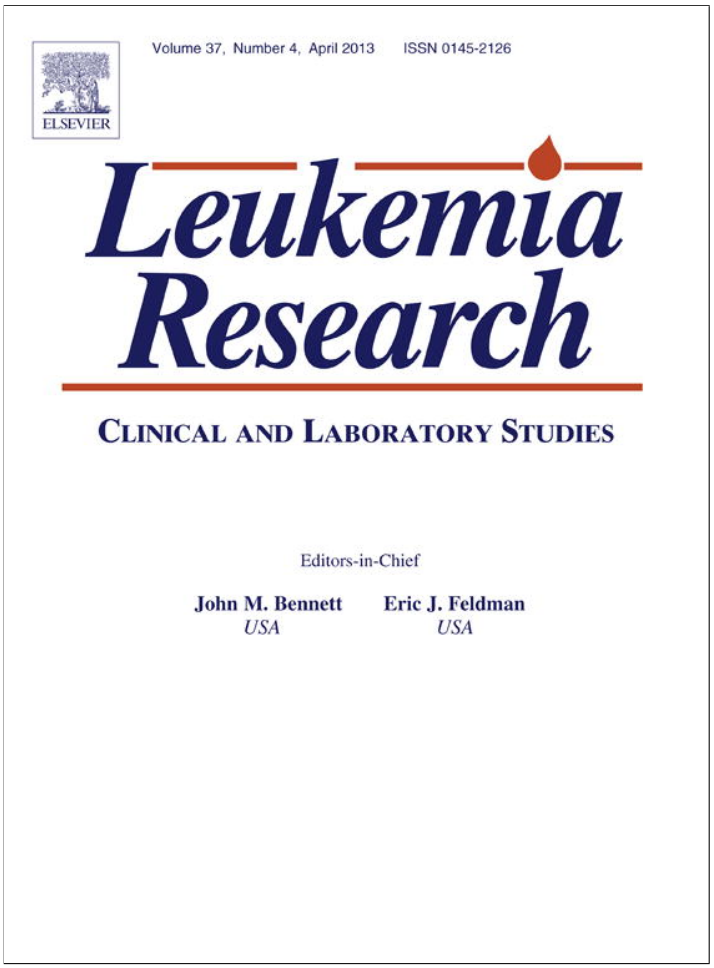
Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright

Author's personal copy

Leukemia Research 37 (2013) 386–391

Contents lists available at SciVerse ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Similar outcomes in Asian and Western patients with diffuse large B-cell lymphoma treated with R-CHOP

Jorge J. Castillo[a,*], Natalie Sinclair[a], Brady E. Beltrán[b], Moo-Kon Song[c], Ivana Ilic[d], Sirpa Leppa[e], Heidi Nurmi[e], Ritsuko Seki[f], Silvia Uccella[g], Jun-Min Li[h], Diana O. Treaba[i], Dariusz Stachurski[i], James N. Butera[a]

[a] Division of Hematology and Oncology, Rhode Island Hospital/The Miriam Hospital, Providence, RI, USA
[b] Department of Oncology and Radiotherapy, Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru
[c] Department of Hematology, Pusan National University Hospital, Pusan, South Korea
[d] Department of Pathology and Cytology, University Hospital Center Zagreb, Zagreb, Croatia
[e] Department of Oncology, Helsinki University Central Hospital, Helsinki, Finland
[f] Kyushu Lymphoma Study Group, Kurume University School of Medicine, Kurume, Japan
[g] Department of Surgical and Morphological Sciences, Pathology Unit, University of Insubria, Varese, Italy
[h] Department of Hematology, Ruijin Hospital, Shanghai, China
[i] Department of Pathology, Rhode Island Hospital/The Miriam Hospital, Providence, RI, USA

ARTICLE INFO

Article history:
Received 14 September 2012
Received in revised form
28 December 2012
Accepted 4 January 2013
Available online 24 January 2013

Keywords:
DLBCL
Race
Rituximab
Chemoimmunotherapy
R-CHOP

ABSTRACT

Background: Little is known on racial differences in patients with diffuse large B-cell lymphoma (DLBCL). The aim of this retrospective study is to compare characteristics, prognostic factors and outcomes of Asian and Western patients with DLBCL treated with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP).
Methods: Patient-level data was collected from 8 centers. All patients were diagnosed with DLBCL and treated with R-CHOP. Patients were divided into Asian and Western, according to the country of report. Comparisons and univariate/multivariate survival analyses were performed.
Results: 712 patients, 455 Asian and 257 Western patients were included. Westerners were more likely to present with elevated LDH (64% *vs.* 48%, $p < 0.01$) and advanced stage (58% *vs.* 49%, $p < 0.01$). After a median follow-up of 36 months, there was no difference in progression-free (PFS; $p = 0.33$) or overall survival (OS; $p = 0.69$). There were no PFS or OS differences between races when evaluating separately each age-adjusted International Prognostic Index category. In the multivariate analyses, performance status and stage were associated with PFS and OS in both races.
Conclusions: There are no differences in prognostic factors, PFS and OS between Asian and Western patients with DLBCL treated with R-CHOP.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

Diffuse large B-cell lymphoma (DLBCL) is an aggressive but curable subtype of non-Hodgkin lymphoma (NHL) [1]. The combination of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) is considered the standard of care for patients with DLBCL. Rituximab in addition to chemotherapy yields improved response rates and survival in patients with newly diagnosed DLBCL [2–4]. Despite the improved response rates there remains a large molecular heterogeneity among patients with DLBCL [5–7], which not surprisingly translates to marked clinical variability.

It is currently unclear if Asian patients present with similar clinical characteristics as Western patients. Few reports have shown that Asian patients may have a higher proportion of extranodal involvement by DLBCL [8]. It has also been suggested that Asian have higher rates of non-germinal center (GC) DLBCL than Western patients [9,10]. Both of these factors could affect outcome in DLBCL patients. Overall, there have not been comparative studies focusing on the racial differences in characteristics at presentation, prognosis and treatment outcomes of DLBCL treated with R-CHOP.

The aim of our retrospective study is to compare the clinicopathological characteristics, prognostic factors and outcomes of Asian and Western patients with a diagnosis of newly diagnosed DLBCL treated with R-CHOP.

* Corresponding author at: 164 Summit Ave, Providence, RI 02906, USA. Tel.: +1 401 793 7151; fax: +1 401 793 7132.
E-mail address: jcastillo@lifespan.org (J.J. Castillo).

0145-2126/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.leukres.2013.01.002

Author's personal copy

2. Patients and methods

2.1. Case selection

The study was approved by the Institutional Review Boards at each of the 8 participating centers from the United States, Finland, Croatia, Italy, Peru, Japan, Korea and China [11–17]. Inclusion criteria were *de novo* pathologically confirmed DLBCL with adequate paraffin block for pertinent studies and a complete follow-up for treatment and outcome. All the patients received at least 6 cycles of R-CHOP every 3 weeks with curative intent. Exclusion criteria were primary mediastinal, CNS or cutaneous DLBCL, transformation from a low-grade NHL and HIV infection. All the patients included were treated after 2002. All the cases were consecutive and underwent clinical staging with at least computed tomography scans and a bone marrow biopsy. Patient-level data included age at diagnosis, sex, performance status according to the Eastern Cooperative Oncology Group (ECOG) scale, lactate dehydrogenase (LDH) levels, number of extranodal sites, Ann Arbor clinical stage, IPI and age-adjusted IPI (aaIPI) score, expression of CD10, BCL6 and MUM1/IRF4 by the tumor cells, response to chemotherapy, progression-free and overall survival (PFS and OS, respectively) in months and final outcome.

In addition to the cases submitted by outside researchers, previously untreated adult patients diagnosed with DLBCL from January 2002 to December 2008 and received therapy with R-CHOP were identified from the medical records of The Miriam and Rhode Island Hospitals in Providence, RI. Pathological samples of the selected patients were retrieved and immunohistochemical staining was performed after deparaffinization in each case. According to the classification proposed by Hans et al. [18], each case was assigned as germinal center (GC) or non-GC; CD10, BCL6 and MUM1/IRF4 expression was considered positive if at least 30% of the tumor cells stained with the antibody. Same cutoffs were used to classify the cases submitted by outside researchers. Additionally, a second look study was performed to assess potential inter-interpreter variability on evaluating the expression of CD10, BCL6 and MUM1/IRF4 [17].

2.2. Statistical analysis

The patients were divided into Asian or Western according to country of report. Clinicopathological characteristics were dichotomized and compared using the Chi-square test. Continuous variables were compared using the Mann–Whitney test. PFS was defined as the time elapsed between date of diagnosis and progression, death or last follow-up. OS was defined as the time elapsed between date of diagnosis and date of death or last follow-up. The Kaplan–Meier method was used to calculate the survival curves, which were compared using the log-rank test. For the multivariate survival analysis, the Cox proportional hazard regression test was used. *P*-values <0.05 were considered statistically significant. All graphics and calculations were obtained using the statistical software MedCalc® (Mariakerke, Belgium) and STATA 12.1 (Statacorp, College Station, TX).

3. Results

3.1. Patients' characteristics

A total of 712 patients, 455 Asian and 257 Western were included in this study. Among all patients, the median age was 64 years (range: 18–90 years) with 52% presenting with advanced stage disease and 55% with elevated LDH. Overall, 81% had a complete response (CR) to six cycles of R-CHOP chemotherapy. Western patients were more likely to present with elevated LDH levels and advanced clinical stage, and were more likely to have high and high-intermediate risk aaIPI scores. There were no differences in age, sex, performance status, number of extranodal sites or response to R-CHOP. Complete group characteristics and comparisons are shown in Table 1.

3.2. Survival analysis and prognostic factors

After a median follow-up time of 36 months, the median PFS and OS were not reached and the 5-year PFS and OS were 57% and 65%, respectively (Fig. 1A and B). Median PFS and OS were not reached and there was no difference in 5-year PFS and OS rates between Asians and Westerners (Fig. 1C and D). In the univariate analysis among Westerners, ECOG performance status >1, elevated LDH and advanced stage were associated with a worse PFS and OS. Among Asians, ECOG performance status >1, >1 extranodal site and advanced stage were significant adverse factors for PFS and OS. In the multivariate analysis, ECOG > 1 and advanced clinical stage were independent prognostic factors associated with a worse OS in both groups. Complete survival analyses are shown in Tables 2 and 3, for Westerners and Asian patients, respectively. Based on these results, we evaluated the aaIPI score in Asian and Western patients. The aaIPI score was prognostic of PFS and OS for both groups of patients ($p < 0.01$ for both, Fig. 2A–D).

When comparing the PFS and OS curves between Asian and Western patients per each of the 4 aaIPI categories, there were no statistically significant differences (data not shown). To further evaluate the lack of difference in survival between Asian and Western patients, we constructed 3 separate Cox hazard models. In the first model, we stratified patients by aaIPI score (4 strata). In the second model, we stratified patients by aaIPI score and sex (8 strata). In the third model, we stratified patients by the aaIPI score, sex and immunohistochemical profile (16 strata), allowing for the highest level of matching between groups. None of the models showed a difference in hazard between Asian and Western patients (data not shown).

4. Discussion

The results of this retrospective multi-center study of over 700 patients support that there are no differences in outcomes between Asian and Western patients with DLBCL treated with R-CHOP. Furthermore, this analysis confirms that well-known risk factors such as clinical stage and performance status appear to be prognostic for survival in Asians as well as Westerners. Most of the research on racial disparities in patients with DLBCL derived from population-based datasets such as the Surveillance, Epidemiology and End Results (SEER) database [19–23]. However, the SEER database does not collect important data regarding clinicopathological characteristics or therapy, and data are restricted to locations within the United States. To the best of our knowledge, this is the first study to compare characteristics, response, survival, and prognostic factors between Asian and Western patients with *de novo* DLBCL who were diagnosed and treated with a uniform regimen in their own countries.

Based on our observations, a higher proportion of Western patients presented with elevated LDH and advance stage, which are consistent with the higher aaIPI scores seen in this population. One could theorize that the range of normality of LDH levels varies from institution to institution; however, our study used "elevated LDH" as a categorical variable based on the range of normality within each institution. Regarding stage, the higher proportion of Western patients diagnosed at a higher stage could be explained by a difference in the use of imaging studies such as positron emission

Author's personal copy

Table 1
Main characteristics of 712 patients with DLBCL treated with R-CHOP according to ethnicity.

Characteristic	All patients 712 (100%)	Western 257 (36%)	Asian 455 (64%)	*p* –
Age (*n* = 712)				
Median (range)	64 (18–90)	63 (18–87)	64 (20–90)	0.13
>60 years	433 (61%)	150 (58%)	283 (62%)	0.31
<60 years	279 (39%)	107 (42%)	172 (38%)	
Sex (*n* = 712)				
Male	386 (54%)	139 (54%)	247 (54%)	0.96
Female	326 (46%)	118 (46%)	208 (46%)	
Performance status (*n* = 709)				
ECOG >1	156 (23%)	61 (24%)	98 (22%)	0.45
ECOG 0–1	513 (77%)	193 (76%)	357 (78%)	
LDH levels (*n* = 707)				
Elevated	369 (55%)	161 (64%)	220 (48%)	<0.01
Normal	298 (45%)	91 (36%)	235 (52%)	
Number extranodal sites (*n* = 709)				
>1 site	102 (15%)	43 (17%)	70 (15%)	0.59
0–1 sites	567 (85%)	211 (83%)	385 (85%)	
Clinical stage (*n* = 712)				
Advanced (III & IV)	372 (52%)	150 (58%)	222 (49%)	0.01
Early (I & II)	340 (48%)	107 (42%)	233 (51%)	
Immunohistochemical profile (*n* = 712)				
Non-germinal center	361 (51%)	136 (53%)	224 (49%)	0.35
Germinal center	351 (49%)	121 (47%)	231 (51%)	
Age-adjusted IPI score (*n* = 705)				
Low risk	136 (19%)	43 (17%)	93 (20%)	<0.01
Low-intermediate risk	291 (41%)	84 (34%)	207 (45%)	
High-intermediate risk	221 (31%)	89 (36%)	132 (29%)	
High risk	57 (8%)	34 (14%)	23 (5%)	
Response to therapy (*n* = 708)				
Complete response	576 (81%)	208 (81%)	343 (76%)	0.12
Partial response	83 (12%)	25 (10%)	69 (15%)	
No response	49 (7%)	23 (9%)	40 (9%)	

ECOG: Eastern Central Oncology Group; LDH: Lactate dehydrogenase; IPI: International Prognostic Index.

tomography, which has a more widespread use, for example, in the United States. Stage 4 disease is defined by extranodal involvement but there was no difference, however, between the proportion of Asian or Western patients with >1 extranodal site involved. All these differences could be explained by an inherent biological difference between races or due to selection bias introduced by our study design. For these reasons, such observations should be considered preliminary.

Approximately 2000 patients were included in the pivotal multi-center study in which the IPI score was developed and validated [24]. However, all the patients were from centers in the United States, Canada and Europe. Furthermore, rituximab was not commercially available at the time of the study. Hence, until recently it was unclear if the IPI was valid in the rituximab era. However, more recent studies have shown that the IPI score remains the most important prognostic tool in patients with *de novo* DLBCL

Table 2
Survival analysis in 257 Western patients with DLBCL treated with R-CHOP.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Progression-free survival				
Age >60 years	0.85 (0.56–1.29)	0.44	0.77 (0.50–1.17)	0.22
Male sex	1.42 (0.94–2.13)	0.10	1.24 (0.81–1.91)	0.32
ECOG >1	1.94 (1.16–3.24)	<0.01	1.59 (1.02–2.50)	0.04
Elevated LDH	1.83 (1.20–2.78)	<0.01	1.44 (0.89–2.34)	0.14
>1 EXN site	2.52 (1.42–4.49)	<0.01	2.06 (1.28–3.33)	<0.01
Advanced stage	1.99 (1.32–2.99)	<0.01	1.51 (0.94–2.45)	0.09
NGC profile	1.17 (0.78–1.75)	0.45	1.05 (0.69–1.59)	0.83
Overall survival				
Age >60 years	0.92 (0.57–1.49)	0.74	0.95 (0.58–1.56)	0.84
Male sex	1.44 (0.90–2.31)	0.14	1.41 (0.85–2.34)	0.18
ECOG >1	2.52 (1.40–4.52)	<0.01	2.10 (1.26–3.49)	<0.01
Elevated LDH	2.66 (1.63–4.34)	<0.01	2.10 (1.13–3.90)	0.02
>1 EXN site	1.34 (0.72–2.51)	0.31	0.89 (0.48–1.67)	0.72
Advanced stage	2.42 (1.50–3.89)	<0.01	1.81 (1.02–3.21)	0.04
NGC profile	1.27 (0.79–2.04)	0.32	1.14 (0.70–1.85)	0.60

HR: Hazard ratio; CI: Confidence interval; ECOG: Eastern Central Oncology Group; LDH: Lactate dehydrogenase; EXN: Extranodal; NGC: Non-germinal center.

Author's personal copy

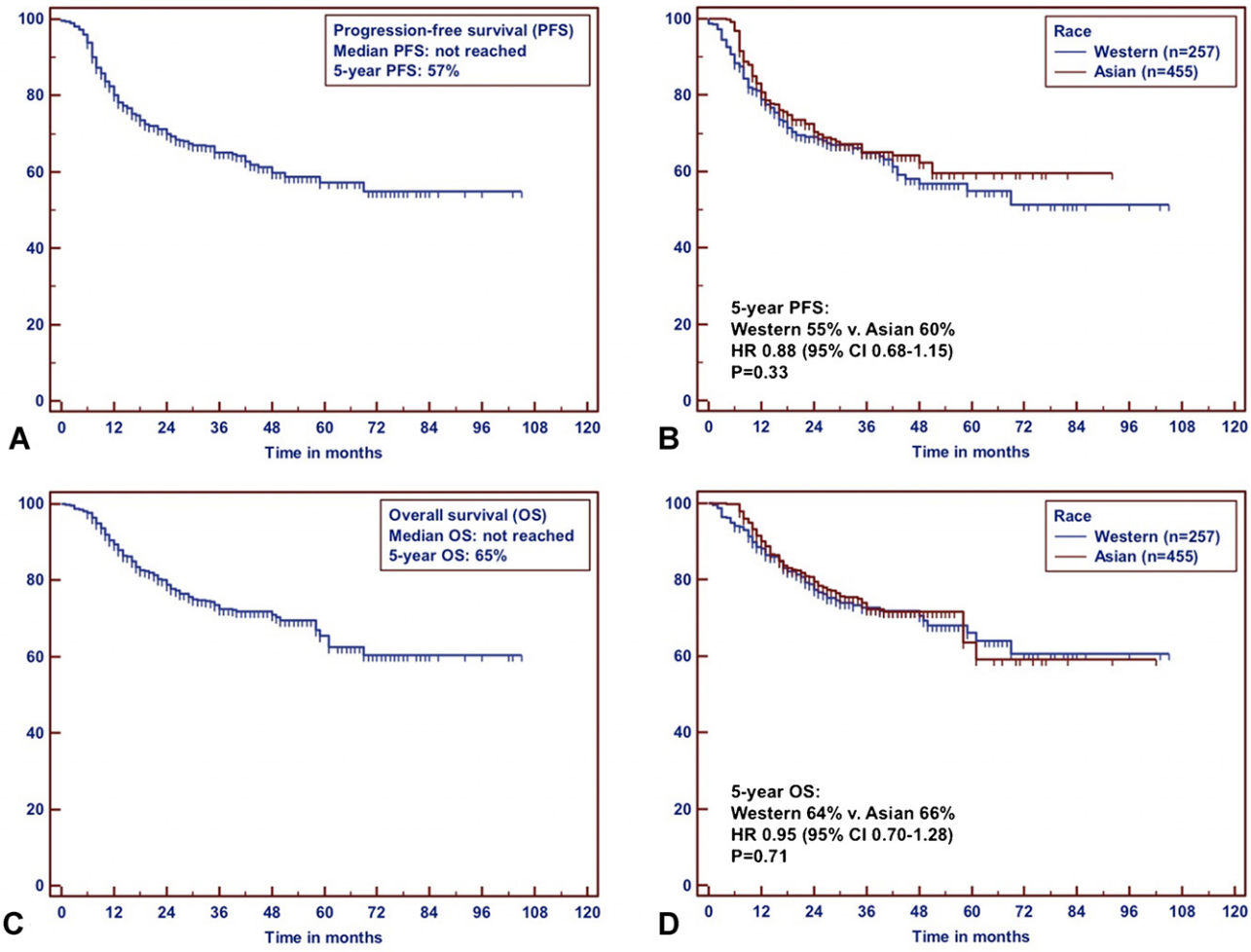


Fig. 1. Kaplan–Meier estimates for 712 patients with DLBCL treated with R-CHOP for progression-free and overall survival for the whole group (A and C, respectively), and according to race (B and D, respectively).

treated in the rituximab era [25]. Our study shows that the IPI distribution was statistically different between Asian and Western patients, due to an increased proportion of Western patients with elevated LDH levels and advanced stage. Despite this difference in IPI distribution, the survival curves for each IPI score did not differ between Asian and Western patients. Even after performing stratified hazard analyses, a survival difference between races could not be detected. A potential explanation could be that elevated LDH did not seem to be of prognostic value for PFS or OS in our cohort of patients, moving our hazard calculations toward the unity. It is

Table 3
Survival analysis in 455 Asian patients with DLBCL treated with R-CHOP.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Progression-free survival				
Age >60 years	1.42 (1.02–1.97)	0.04	1.49 (1.05–2.13)	0.03
Male sex	1.09 (0.79–1.51)	0.61	1.18 (0.85–1.63)	0.34
ECOG >1	2.80 (1.82–4.29)	<0.01	2.12 (1.47–3.05)	<0.01
Elevated LDH	0.90 (0.65–1.24)	0.52	1.18 (0.84–1.66)	0.34
>1 EXN site	2.32 (1.43–3.77)	<0.01	1.41 (0.93–2.12)	0.11
Advanced stage	2.52 (1.82–3.49)	<0.01	2.01 (1.37–2.93)	<0.01
NGC profile	1.13 (0.82–1.56)	0.46	1.12 (0.81–1.56)	0.50
Overall survival				
Age >60 years	1.35 (0.93–1.97)	0.13	1.51 (1.01–2.28)	0.05
Male sex	1.30 (0.89–1.88)	0.17	1.18 (1.00–2.18)	0.05
ECOG >1	3.31 (2.04–5.35)	<0.01	2.46 (1.64–3.70)	<0.01
Elevated LDH	0.82 (0.57–1.19)	0.30	1.15 (0.77–1.70)	0.50
>1 EXN site	2.38 (1.38–4.10)	<0.01	1.32 (0.84–2.10)	0.23
Advanced stage	3.20 (2.21–4.65)	<0.01	2.51 (1.60–3.96)	<0.01
NGC profile	1.21 (0.84–1.76)	0.31	1.20 (0.82–1.75)	0.36

HR: Hazard ratio; CI: Confidence interval; ECOG: Eastern Central Oncology Group; LDH: Lactate dehydrogenase; EXN: Extranodal; NGC: Non-germinal center.

Author's personal copy

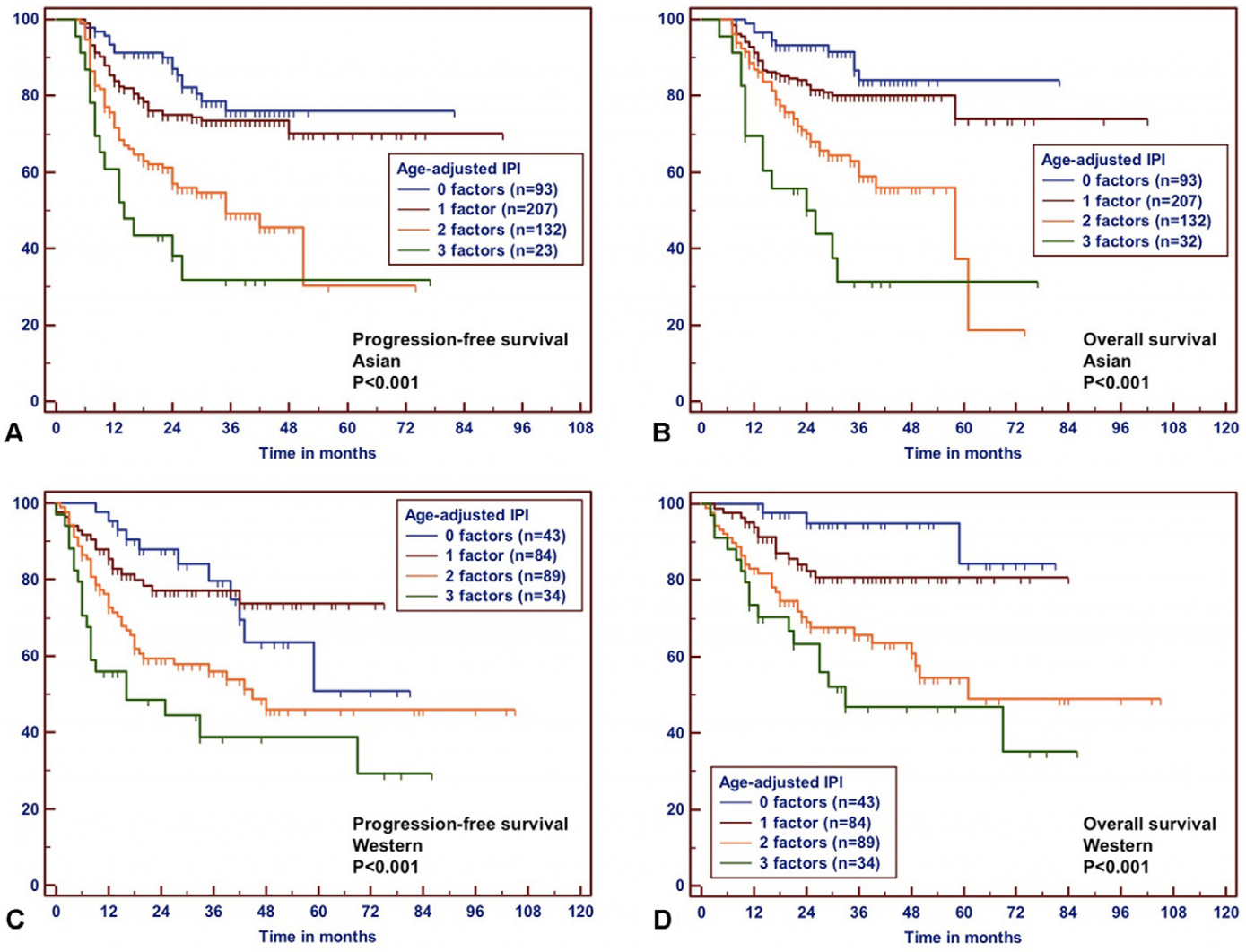


Fig. 2. Kaplan–Meier estimates for progression-free and overall survival in Asian (A and C, respectively) and Western DLBCL patients (B and D, respectively) according to the age-adjusted International Prognostic Index score.

also possible that with longer follow-up, a difference in OS could become evident.

Our study showed no difference in the proportion of GC or non-GC DLBCL between races. This analysis adds to the current data, which is however inconsistent regarding the proportion of GC or non-GC DLBCL in Asian populations. Some studies report a higher proportion of GC DLBCL while others report a higher proportion of non-GC DLBCL in Asian individuals [9,10,26,27]. Potential explanations for these findings are our relatively small sample size and selection bias, which could have been introduced given the retrospective nature of our study. It is important to note, however, that our study included consecutive patients at each of the participating institutions and that a portion of the pathological samples was evaluated for consistency. Importantly, we used the algorithm proposed by Hans to classify our patients as GC or non-GC DLBCL [18]; however, there are mounting data arguing against the utility of immunohistochemical classifiers given the lack of concordance between pathologists [17,28]. To date, a series of algorithms have been developed in attempts to reflect the results of molecular studies [29]. It is unclear if a difference in the proportion of GC and non-GC DLBCL between Asian and Western patients could be identified if molecular and/or genomic-based studies were performed. For this purpose, large population-based studies with centralized pathological evaluation and molecular and/or genomic confirmation are needed to clarify this point.

In conclusion, our study suggests that there is no difference in survival between Asian and Western patients with newly diagnosed DLBCL treated with R-CHOP. However, patient-centered outcomes research evaluating racial differences is warranted.

Conflict of interest statement

The authors have no conflict of interest to disclose.

Acknowledgements

Preliminary results from this study were presented at the Lymphoma & Myeloma 2011 in New York, New York, October 20-22, 2011, and the 53rd American Society of Hematology Annual Meeting in San Diego, California, December 10–13, 2011.

Funding: There were no specific funding sources for this study.

Authors' contributions: Conception and design of the study: JJC acquisition, analysis and interpretation of data: JJC,NS, BEB, MKS, II, SL, HN, RS, SU, JML, DOT, DS, JNB. Manuscript writing: JJC, JNB. Final approval of the manuscript: JJC,NS, BEB, MKS, II, SL, HN, RS, SU, JML, DOT, DS, JNB.

Author's personal copy

References

[1] Stein H, Warnke R, Chan W, et al. Diffuse large B-cell lymphoma, not otherwise specified. In: Swerdlow S, et al., editors. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: IARC; 2008. p. 233–7.

[2] Feugier P, Van Hoof A, Sebban C, et al. Long-term results of the R-CHOP study in the treatment of elderly patients with diffuse large B-cell lymphoma: a study by the Groupe d'Etude des Lymphomes de l'Adulte. J Clin Oncol 2005;23:4117–26.

[3] Pfreundschuh M, Trumper L, Osterborg A, et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group. Lancet Oncol 2006;7:379–91.

[4] Habermann TM, Weller EA, Morrison VA, et al. Rituximab-CHOP versus CHOP alone or with maintenance rituximab in older patients with diffuse large B-cell lymphoma. J Clin Oncol 2006;24:3121–7.

[5] Lenz G, Wright G, Dave SS, et al. Stromal gene signatures in large-B-cell lymphomas. N Engl J Med 2008;359:2313–23.

[6] Alizadeh AA, Eisen MB, Davis RE, et al. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. Nature 2000;403:503–11.

[7] Rosenwald A, Wright G, Chan WC, et al. The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. N Engl J Med 2002;346:1937–47.

[8] Ke X, Wang J, Gao Z, et al. Clinical characteristics and prognostic analysis of Chinese patients with diffuse large B-cell lymphoma. Blood Cells Mol Dis 2010;44:55–61.

[9] Shia AK, Gan GG, Jairaman S, et al. High frequency of germinal centre derivation in diffuse large B cell lymphoma from Asian patients. J Clin Pathol 2005;58:962–7.

[10] Shiozawa E, Yamochi-Onizuka T, Takimoto M, et al. The GCB subtype of diffuse large B-cell lymphoma is less frequent in Asian countries. Leuk Res 2007;31:1579–83.

[11] Ilic I, Mitrovic Z, Aurer I, et al. Lack of prognostic significance of the germinal-center phenotype in diffuse large B-cell lymphoma patients treated with CHOP-like chemotherapy with and without rituximab. Int J Hematol 2009;90:74–80.

[12] Nyman H, Adde M, Karjalainen-Lindsberg ML, et al. Prognostic impact of immunohistochemically defined germinal center phenotype in diffuse large B-cell lymphoma patients treated with immunochemotherapy. Blood 2007;109:4930–5.

[13] Seki R, Ohshima K, Fujisaki T, et al. Prognostic impact of immunohistochemical biomarkers in diffuse large B-cell lymphoma in the rituximab era. Cancer Sci 2009;100:1842–7.

[14] Song MK, Chung JS, Seol YM, et al. Influence of low absolute lymphocyte count of patients with nongerminal center type diffuse large B-cell lymphoma with R-CHOP therapy. Ann Oncol 2010;21:140–4.

[15] Uccella S, Placidi C, Marchet S, et al. Bcl-6 protein expression, and not the germinal centre immunophenotype, predicts favourable prognosis in a series of primary nodal diffuse large B-cell lymphomas: a single centre experience. Leuk Lymphoma 2008;49:1321–8.

[16] Xia ZG, Xu ZZ, Zhao WL, et al. The prognostic value of immunohistochemical subtyping in Chinese patients with de novo diffuse large B-cell lymphoma undergoing CHOP or R-CHOP treatment. Ann Hematol 2010;89:171–7.

[17] Castillo JJ, Beltran BE, Song MK, et al. The Hans algorithm is not prognostic in patients with diffuse large B-cell lymphoma treated with R-CHOP. Leuk Res 2012;36:413–7.

[18] Hans CP, Weisenburger DD, Greiner TC, et al. Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray. Blood 2004;103:275–82.

[19] Carreon JD, Morton LM, Devesa SS, et al. Incidence of lymphoid neoplasms by subtype among six Asian ethnic groups in the United States, 1996–2004. Cancer Causes Control 2008;19:1171–81.

[20] Griffiths R, Gleeson M, Knopf K, et al. Racial differences in treatment and survival in older patients with diffuse large B-cell lymphoma (DLBCL). BMC Cancer 2010;10:625.

[21] Komrokji RS, Al Ali NH, Beg MS, et al. Outcome of diffuse large B-Cell lymphoma in the United States has improved over time but racial disparities remain: review of SEER data. Clin Lymphoma Myeloma Leuk 2011;11:257–60.

[22] Shenoy PJ, Malik N, Nooka A, et al. Racial differences in the presentation and outcomes of diffuse large B-cell lymphoma n the United States. Cancer 2010.

[23] Wu XC, Andrews P, Chen VW, et al. Incidence of extranodal non-Hodgkin lymphomas among whites, blacks, and Asians/Pacific Islanders in the United States: anatomic site and histology differences. Cancer Epidemiol 2009;33:337–46.

[24] A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993;329:987–94.

[25] Ziepert M, Hasenclever D, Kuhnt E, et al. Standard International prognostic index remains a valid predictor of outcome for patients with aggressive CD20+ B-cell lymphoma in the rituximab era. J Clin Oncol 2010;28:2373–80.

[26] Chen Y, Chen H, Fu K, et al. Prevalence of germinal center B-cell-like and non-germinal center B-cell-like types of diffuse large B-cell lymphoma in Shanghai, China. Zhonghua Bing Li Xue Za Zhi 2010;39:313–8.

[27] Li T, Medeiros LJ, Lin P, et al. Immunohistochemical profile and fluorescence in situ hybridization analysis of diffuse large B-cell lymphoma in northern China. Arch Pathol Lab Med 2010;134:759–65.

[28] de Jong D, Rosenwald A, Chhanabhai M, et al. Immunohistochemical prognostic markers in diffuse large B-cell lymphoma: validation of tissue microarray as a prerequisite for broad clinical applications—a study from the Lunenburg Lymphoma Biomarker Consortium. J Clin Oncol 2007;25:805–12.

[29] Meyer PN, Fu K, Greiner TC, et al. Immunohistochemical methods for predicting cell of origin and survival in patients with diffuse large B-cell lymphoma treated with rituximab. J Clin Oncol 2011;29:200–7.