

Original Article

# Treatment Outcome of Adult Burkitt Lymphoma in Japanese Patients with Modified LMB Protocol : A Single Center Retrospective Analysis

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The prognosis of adult Burkitt lymphoma (BL) has improved in western countries since the introduction of high-dose methotrexate (HD-MTX)-containing chemotherapy. Here we analyzed nine consecutive Japanese patients diagnosed with BL at our institution. All except for the three elderly (> 70 years) patients were treated with a regimen including 13 g/m<sup>2</sup> HD-MTX in total, divided into 3 cycles. The median follow-up period was 56 months (range 38-118). All the nine patients achieved complete remission and have not shown any disease progression, including the three elderly patients who received reduced doses or alternative treatments. These observations suggest that chemotherapy including 13 g/m<sup>2</sup> HD-MTX in total is tolerable and effective in Japanese adult BL patients aged < 70 and that BL is curable even if developed in those who are > 70 years. [*J Clin Exp Hematopathol* 51(2) : 109-114, 2011]

**Keywords:** Burkitt lymphoma, high-dose methotrexate, World Health Organization classification

## INTRODUCTION

Burkitt lymphoma (BL) is a rare, highly aggressive B-cell lymphoma that preferentially occurs in children and young adults.<sup>1,2</sup> Despite its highly aggressive course, the prognosis of BL has improved after the introduction of rapidly cycling, intensive chemotherapy regimens such as the “LMB (Lymphoma Malignancy B) protocol” (originally reported by a French group) and “CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, methotrexate/ifosfamide, etoposide, and cytarabine) therapy” that include high-dose methotrexate (HD-MTX).<sup>3-5</sup> However, most of the studies testing these regimens were performed in European and North American

populations and their suitability for other populations remains to be determined.

Here, we report, after re-evaluation of diagnosis based on version 4 (v4) of the World Health Organization (WHO) classification, a retrospective analysis of eleven consecutive Japanese patients who were diagnosed with BL or B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma (iDLBCL/BL) and treated with an LMB-like regimen.

## PATIENTS AND METHODS

### *Patients and re-evaluation*

We reviewed the clinical records at Tsukuba University Hospital between 1996 and 2009, and identified 12 and 1 patients who, according to the v3 WHO classification, had been diagnosed with BL and Burkitt-like lymphoma (BLL), respectively (Table 1). One BL patient diagnosed in 1996 was excluded from this analysis because he received allogeneic stem cell transplantation after chemotherapy. Another BL patient was positive for human immunodeficiency virus (HIV) and was also excluded from the analysis. Thus, 10 BL and 1 BLL consecutive cases, all of which were negative for HIV, were re-evaluated for diagnosis on the basis of the v4

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**Table 1.** Clinical features, diagnosis according to the v3 WHO classification, stage, and survival of the patients

Case No.	Age/Sex	Main lesion	Bulky	CNS	BM	Stage	PS $\geq$ 2	Initial diagnosis	CR	Current status	Follow up period (months)
1	46/F	jaw, stomach	+	-	-	III	Yes	BL	Yes	Alive	118
2	70/M	salivary gland	+	-	-	II	Yes	BL	Yes	Alive	112
3	65/F	salivary gland, stomach	+	-	-	III	Yes	BL	Yes	Alive	103
4	73/M	salivary gland	+	-	+	IV	Yes	BL	Yes	Alive	38
5	16/M	paraaorta, axillary	+	+	-	IV	No	BL	Yes	Alive	56
6	20/F	ovary, paraaorta	+	-	-	IV	Yes	BL	Yes	Alive	56
7	82/M	paraaorta, mediastinum	+	-	+	III	Yes	BL	Yes	Alive	41
8	54/M	pharynx	-	-	-	I	Yes	BL	Yes	Alive	38
9	40/F	ovary, paraaorta	+	-	-	III	No	BL	Yes	Alive	60
10	39/F*	ovary, paraaorta	+	-	-	IV	Yes	BLL	No	Death	3
11	42/M*	salivary gland, stomach	+	+	-	IV	Yes	BL	Yes	CNS relapse Death	7

The clinical stage of each case was defined by the Ann Arbor staging system. BL; Burkitt lymphoma, BLL; Burkitt-like lymphoma,\*; Two patients were diagnosed as iDLBCL/BL after re-evaluation according to the v4 classification.

### WHO classification.

For the re-evaluation, hematoxylin-eosin-stained specimens were reviewed by two pathologists who were not involved in the initial diagnosis. Immunocytochemical stainings of paraffin sections were added to evaluate the expression of CD10, CD20, BCL2, BCL6, MUM1, and Ki-67. Rearrangement of the *cMYC* and *BCL2* genes was studied by interphase fluorescence *in situ* hybridization (FISH) on thin-sliced paraffin sections. The probes used for FISH were Dual Fusion Translocation Probe IGH SG/MYC SO [for t(8;14); Vysis, Richmond, United Kingdom], BCL2 FISH DNA Probe Split Signal and MYC FISH DNA Probe Split Signal [for (14;18), and t(8;14) and t(2;8), respectively; DAKO, Carpinteria, CA, USA].<sup>6</sup>

The clinical stage of each case was defined by the Ann Arbor staging system. The bulky mass was defined as a tumor with a diameter of at least 10 cm.

### Treatment

The 6BL patients who were < 70 years, as well as 2 iDLBCL/BL patients, were treated with intensive chemotherapy based on the LMB protocol as summarized in Fig. 1 (modified LMB protocol).<sup>7-10</sup> The doses of cyclophosphamide (CPA) in induction therapy, and cytarabine (AraC) and etoposide (VP-16) in consolidation #1 were reduced compared with those in the original LMB protocol. AraC in original consolidation #2 was also changed to VP-16 on days 3-6.<sup>10</sup> The induction regimen consisted of MTX (5,000 mg/m<sup>2</sup>) on day 1, CPA (1,000 mg/m<sup>2</sup>) on days 2 and 3, adriamycin (ADR, 60 mg/m<sup>2</sup>) on day 2, vincristine (VCR, 1.4 mg/m<sup>2</sup>) on days 1 and 7, prednisolone (PSL, 60 mg/m<sup>2</sup>) on days 1-10, and granulocyte colony-stimulating factor (G-CSF, 5  $\mu$ g/m<sup>2</sup>) on day 5, which was continued until absolute white blood cell count of > 5.0  $\times$  10<sup>3</sup>/mL with > 50% neutro-

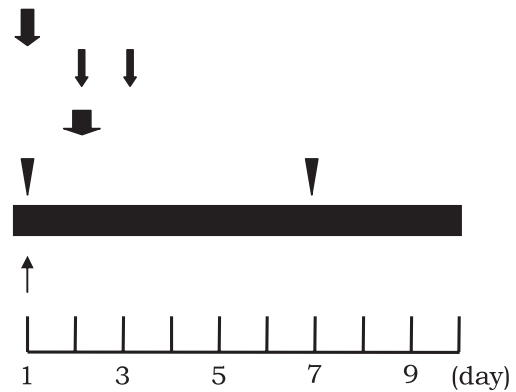
phils was achieved. As CNS prophylaxis, intrathecal therapy (IT) consisting of AraC (40 mg), MTX (15 mg), and PSL (20 mg) was applied on day 1. CNS prophylactic irradiation was not included at any point in the treatment plan. Leukovorin rescue was commenced 2 hr after the completion of HD-MTX administration and continued until the serum MTX level was decreased to < 5  $\times$  10<sup>-8</sup> M. This regimen was repeated once for all patients. The 3 elderly BL patients principally received the same regimen except that the dose of MTX was reduced to 1,000 mg/m<sup>2</sup>. To keep the intervals between regimens as short as possible, the next regimen was started when absolute neutrophil counts of > 1.5  $\times$  10<sup>3</sup>/mL and platelet counts of > 10  $\times$  10<sup>4</sup>/mL were achieved. For patients with a bulky mass or a poor general condition, pre-phase therapy with PSL alone, COP (CPA, VCR, and PSL), or CHOP (CPA, VCR, ADR, and PSL) was performed before induction therapy.

After complete remission (CR) or uncertain remission (CRu) was confirmed, and if absolute neutrophil and platelet counts were over 1.5  $\times$  10<sup>3</sup>/mL and 10  $\times$  10<sup>4</sup>/mL, respectively, the consolidation #1 regimen was started. This regimen consisted of IT on days 1 and 6, AraC (2,000 mg/m<sup>2</sup>  $\times$  2) on days 3-5, and VP-16 (100 mg/m<sup>2</sup>) on days 3-6. Rituximab (375 mg/m<sup>2</sup>) was added to the consolidation #1 regimen (on day 1) for patients who were diagnosed after April, 2006.

If absolute neutrophil and platelet counts were over 1.5  $\times$  10<sup>3</sup>/mL and 10  $\times$  10<sup>4</sup>/mL, respectively, the consolidation #2 regimen was started. This regimen consisted of IT on days 1 and 6, MTX (3,000 mg/m<sup>2</sup>) on day 3, and VP-16 (60 mg/m<sup>2</sup>) on days 3-6. Rituximab (375 mg/m<sup>2</sup>) was added to the consolidation #2 regimen (on day 1) for patients who were diagnosed after April, 2006. G-CSF was used during neutropenia (< 500/mm<sup>3</sup>).

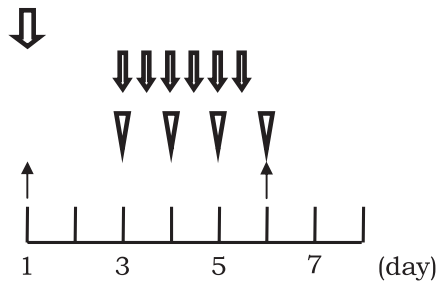
**Induction protocol**

Methotrexate: 5,000 mg/m<sup>2</sup>, 6 hr, DIV day 1  
 Cyclophosphamide: 1,000 mg/m<sup>2</sup>, 2 hr, DIV day 2,3  
 Adriamycin: 60 mg/m<sup>2</sup>, IV, day 2  
 Vincristine: 1.4 mg/m<sup>2</sup>, IV, day 1,7  
 Prednisolone: 60 mg/m<sup>2</sup>, IV or PO, day 1-10  
 IT\*: day 1



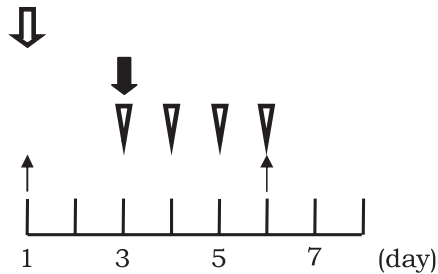
**Consolidation # 1**

Rituximab: 375 mg/m<sup>2</sup>, DIV, day 1  
 Cytarabine: 2,000 mg/m<sup>2</sup> x 2, 2.5 hr, DIV, day 3- 5  
 VP-16: 100 mg/m<sup>2</sup>, 1 hr, DIV, day 3- 6  
 IT\*: day 1, 6



**Consolidation # 2**

Rituximab: 375 mg/m<sup>2</sup>, DIV, day 1  
 Methotrexate: 3,000 mg/m<sup>2</sup>, 24 hr, DIV, day 3  
 VP-16: 60mg/m<sup>2</sup>, 1 hr, DIV, day 3- 6  
 IT\*: day 1, 6



**Fig. 1.** Treatment scheme. The induction course was repeated once (2 induction courses in total). IV, intravenous injection; PO, orally; IT\*, intrathecal chemotherapy (cytarabine 40 mg + methotrexate 15 mg + prednisolone 20 mg)

**Assessment of remission and adverse events**

Initial staging and prognosis factors were evaluated by obtaining a medical history, performing a physical examination and standard blood tests, including measurements of lactate dehydrogenase (LDH) and soluble interleukin-2 receptor (sIL-2R) levels, and conducting other examinations as follows: computed tomographic scan of the chest, abdomen, and pelvis; magnetic resonance imaging of the brain and spine; lumbar puncture [if central nervous system (CNS) involvement was suspected]; and bone marrow aspiration and biopsy. All cases were examined for anti-HIV antibody, hepatitis B surface (HBs) antigen, anti-HBs antibody, and hepatis

is C antibody. Elevated serum LDH and sIL-2R levels were defined when greater than 245 U/L and 519 U/mL, respectively. Responses were evaluated according to the guidelines reported by Cheson *et al.*<sup>11</sup> Toxicities and adverse events related to chemotherapy were assessed and graded according to the National Cancer Institute Common Toxicity Criteria, version 2.0.<sup>12</sup>

**RESULTS**

**Re-evaluation based on the v4 WHO classification**

The median age of patients was 46 years (range 16-82),

**Table 2.** Diagnosis and re-evaluation of the patients according to the v4 classification

Case No.	Age/Sex	Starry sky	Ki-67	CD10	CD20	BCL2	BCL6	MUM1	IgH/ <i>cMYC</i>	<i>cMYC</i> split	BCL2 split	G-band	Initial diagnosis (v3)	Reviewed diagnosis (v4)
1	46/F	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
2	70/M	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
3	65/F	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
4	73/M	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
5	16/M	+	≥ 90%	+	+	-	+	+	+	+	-	N. D*	BL	BL
6	20/F	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
7	82/M	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
8	54/M	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
9	40/F	+	≥ 90%	+	+	-	+	-	+	+	-	N. D*	BL	BL
10	39/F	-	≥ 90%	+	+	-	-	-	+	+	-	complex**	BLL	iDLBCL/BL
11	42/M	+	≥ 90%	+	+	+	-	-	+	+	-	N. D*	BL	iDLBCL/BL

The results of the morphological, immunophenotypical, and genetical analysis of the patients were shown. All patients were re-diagnosed according to the v4 classification. N.D.; not determined complex\*\* ; 50 XX, +3, add (6) (q21), del (6) (q?), +7, add (14) (q32), add (17) (q11,2)+18, +mar1

**Table 3.** Laboratory data at diagnosis

Case No.	Age/Sex	WBC ( $\mu\text{L}$ )	Hgb (g/dL)	Plt ( $\times 10^4/\mu\text{L}$ )	LDH (U/L)	CRP (mg/dL)	sIL-2R (U/mL)
1	46/F	4,300	14.1	25.8	299	1.04	571
2	70/M	8,110	13.9	21.4	396	3.42	692
3	65/F	5,400	11.2	29.2	203	0.78	490
4	73/M	4,900	15.9	16.5	929	0.25	753
5	16/M	7,600	17.5	35.0	374	0.08	983
6	20/F	27,900	12.2	58.7	751	29.33	11,826
7	82/M	5,700	14.0	25.4	149	0.01	279
8	54/M	7,400	11.3	24.2	564	2.52	4,560
9	40/F	6,500	9.4	46.0	312	0.47	580
10	39/F*	25,000	9.5	7.9	1,204	9.59	31,328
11	42/M*	4,500	12.3	32.1	1,004	4.03	1,596

WBC; white blood cell count, Hgb; hemoglobin level, Plt; platelet count, LDH; lactate dehydrogenase, CRP; C-reactive protein, sIL-2R; soluble interleukin-2 receptor, \*; Patients with iDLBCL/BL

with 3 patients aged > 70 years. Nine out of 11 patients were in advanced stages (stage III or IV) at the diagnosis. Eight patients exhibited extranodal involvement (Table 1).

When all 11 cases were re-evaluated according to the v4 WHO classification (Table 2), 9 of the 10 cases originally diagnosed as BL showed typical “starry sky” morphology, positive staining for CD20 and BCL6, negative staining for BCL2, > 90% positive for Ki-67 staining, and *cMYC* rearrangement upon FISH analysis. Thus, the diagnosis of BL was unchanged for these cases.

The diagnosis of one (UNP11) of the ten cases whose original diagnosis was BL was changed to iDLBCL/BL because of strongly positive BCL2 staining, despite the fact that all other features were compatible with BL. None of the cases including UNP11 demonstrated *BCL2* rearrangement. The one case originally diagnosed as BLL (UNP10) was re-diagnosed as iDLBCL/BL because of the presence of large B cells that were recognizable as tumor cells, which matched the morphological criteria of iDLBCL/BL.

G-banding analysis in one iDLBCL/BL case (UNP10) showed a complex karyotype, while cytogenetic data were not available in other patients (Table 1).

LDH and sIL-2R levels were elevated in 7 BL patients. Two iDLBCL/BL patients had extranodal involvement with high LDH and sIL2-R levels (Tables 1 & 3).

### Response to therapy and outcome

Of the 11 patients, “prephase” treatment was given to 10 patients (8 BL and 2 iDLBCL/BL) because they had bulky mass, as well as 7 patients (5 BL and 2 iDLBCL/BL) with a poor general condition (Table 1). As the prephase treatment, 5 patients (4 BL and 1 iDLBCL/BL) were given a COP or a CHOP regimen while the remaining 5 patients were given PSL alone.

After the two courses of induction regimen, 10 patients (9 BL and 1 iDLBCL/BL) achieved CR or CRu. All the 9 BL patients maintained progression-free survival for 38-118

months (median 56 months, Table 1). For reasons of old age (UNP 7) and poor general condition (UNP 2), the consolidation regimens were omitted in one case (UNP 7) and both the second induction regimen and the two consolidation regimens were omitted in another case (UNP 2); instead, radiation therapy for the residual lesion was provided. Both patients have shown no signs of relapse and are still alive 3 and 9 years later, respectively.

Both iDLBCL/BL patients died from infection after the first induction therapy and CNS relapse.

### Toxicity of treatment

Myelosuppression was the main form of toxicity. Febrile neutropenia was observed in 7 (63%) patients after first induction regimen. Grade III/IV thrombocytopenia and anemia were observed in 4 (36%) and 2 (18%) patients, respectively (Table 4). Two patients suffered from acute renal dysfunction but recovered without recourse to hemodialysis. Tumor lysis syndrome during and after the first induction regimen was experienced in one iDLBCL/BL patient (UNP 10), who died from peritonitis and sepsis compromised by tumor lysis syndrome despite the prephase (CHOP) therapy.

The incidence of therapy-related toxicity was much lower in the second course of induction regimen than in the first course (grade III/IV thrombocytopenia, 36% vs. 10%; febrile neutropenia, 63% vs. 30% in the first and second courses, respectively; Table 4). However, grade III/IV hematologic toxicities and febrile neutropenia were frequently observed after consolidation #1 (anemia, 77%; thrombocytopenia, 87.5%; febrile neutropenia, 77%). Although grade III mucositis was documented in 36, 20, and 37% after the treatment, which included HD-MTX (first induction, second induction, and consolidation #2, respectively), the median period required for the recovery to the grade II level or less was 5 days. No grade IV mucositis was documented.

There were no obvious additional toxicities in patients who received rituximab.

## DISCUSSION

Intensive chemotherapy regimens that include HD-MTX as well as high-dose AraC and CPA<sup>13</sup> were developed for pediatric BL and later applied to adult BL. This development appears to have improved the prognosis of adult BL.<sup>3-5,8,10,14,15</sup> The effectiveness of LMB protocol for adult BL was reported in 1995,<sup>10</sup> which was one of the earliest reports describing successful treatment of adult BL using HD-MTX. The original CODOX-M/IVAC was also reported by Magrath *et al.* in 1996,<sup>3</sup> although this protocol was modified through clinical studies;<sup>4,5</sup> the reduction of MTX was among major changes because the principal cause of toxicity in the original CODOX-M/IVAC was the use of MTX at 6.7 g/m<sup>2</sup> in a single course. While there is a consensus on the necessity of HD-MTX for BL treatment, the MTX dose and timing are under debate.

Most of the ensuing confirmatory studies, however, in addition to the original LMB and CODOX-M/IVAC studies, were performed with European and North American populations, while a retrospective analysis using LMB protocol for adult BL was previously reported from a Korean group.<sup>7</sup> This raises the question of whether the same results can be produced in Japanese populations. For this reason, we retrospectively analyzed whether a modified LMB protocol in adult Japanese BL patients would be efficient and feasible.

For the 9 patients < 70 years, MTX was given at 5 g/m<sup>2</sup> in the first and second courses of the induction regimen and at 3 g/m<sup>2</sup> in the consolidation #2 regimen, meaning that 13 g/m<sup>2</sup> was delivered in total over 4 courses of chemotherapy. The toxicities during the induction phase were well tolerated, with close monitoring of MTX level in the serum. All the 6 BL patients who received the modified LMB protocol as planned have survived for more than 3 years, which indicates that intensive chemotherapy including MTX at high doses such as 13 g/m<sup>2</sup> in total is both tolerable and effective for Japanese BL patients < 70 years. The LMB-like protocol may be suitable to treat Asian BL patients, as was suggested by a

**Table 4.** Frequency of adverse events during the treatment

Toxicity (%)	Induction 1	Induction 2	Consolidation 1	Consolidation 2
Anemia	18	0	75	11
Thrombocytopenia	36	10	87	0
Febrile neutropenia	63	30	77	11
Mucositis	36*	20	0	37*
Neuropathy	9*	0	0	0
Bilirubin	18*	0	0	0
Renal failure	18	0	0	0
Tumor lysis syndrome	18*	0	0	0

Grade III/IV toxicities and adverse events related to chemotherapy are shown. Toxicities and adverse events related to chemotherapy were assessed and graded according to the National Cancer Institute Common Toxicity Criteria, version 2.0.

\*; No Grade IV toxicity was documented.



previous report from Korea.<sup>7</sup> Our results also suggest that BL could be curable with less intensive chemo-radiotherapy, given that all the 3 elderly patients who received a reduced dose have survived for more than 3 years.

In conclusion, not only the modified CODOX-M/IVAC protocol<sup>16</sup> but also the modified LMB protocol is effective and tolerable in Japanese adult BL patients *aged* < 70. For elderly patients, reduced dose and/or cycles of chemotherapy may be required, and reduced doses could be effective.

**Declaration of interest :** The authors report no conflicts of interest. The authors are responsible for the content and writing of the paper.

## REFERENCES

- 1 Perkins AS, Friedberg JW: Burkitt lymphoma in adults. Hematology Am Soc Hematol Educ Program 341-348, 2008
- 2 Blum KA, Lozanski G, Byrd JC: Adult Burkitt leukemia and lymphoma. Blood 104:3009-3020, 2004
- 3 Magrath I, Adde M, Shad A, Venzon D, Seibel N, *et al.*: Adults and children with small non-cleaved-cell lymphoma have a similar excellent outcome when treated with the same chemotherapy regimen. J Clin Oncol 14:925-934, 1996
- 4 Mead GM, Sydes MR, Walewski J, Grigg A, Hatton CS, *et al.*: An international evaluation of CODOX-M and CODOX-M alternating with IVAC in adult Burkitt's lymphoma: results of United Kingdom Lymphoma Group LY06 study. Ann Oncol 13:1264-1274, 2002
- 5 Mead GM, Barrans SL, Qian W, Walewski J, Radford JA, *et al.*: A prospective clinicopathologic study of dose-modified CODOX-M/IVAC in patients with sporadic Burkitt lymphoma defined using cytogenetic and immunophenotypic criteria (MRC/NCRI LY10 trial). Blood 112:2248-2260, 2008
- 6 Barrans SL, Evans PA, O'Connor SJ, Owen RG, Morgan GJ, *et al.*: The detection of t(14;18) in archival lymph nodes: development of a fluorescence in situ hybridization (FISH)-based method and evaluation by comparison with polymerase chain reaction. J Mol Diagn 5:168-175, 2003
- 7 Choi MK, Jun HJ, Lee SY, Kim KH, Lim do H, *et al.*: Treatment outcome of adult patients with Burkitt lymphoma: results using the LMB protocol in Korea. Ann Hematol 88:1099-1106, 2009
- 8 Divine M, Casassus P, Koscielny S, Bosq J, Sebban C, *et al.*: Burkitt lymphoma in adults: a prospective study of 72 patients treated with an adapted pediatric LMB protocol. Ann Oncol 16:1928-1935, 2005
- 9 Galicier L, Fieschi C, Borie R, Meignin V, Daniel MT, *et al.*: Intensive chemotherapy regimen (LMB86) for St Jude stage IV AIDS-related Burkitt lymphoma/leukemia: a prospective study. Blood 110:2846-2854, 2007
- 10 Soussain C, Patte C, Ostronoff M, Delmer A, Rigal-Huguet F, *et al.*: Small noncleaved cell lymphoma and leukemia in adults. A retrospective study of 65 adults treated with the LMB pediatric protocols. Blood 85:664-674, 1995
- 11 Cheson BD, Horning SJ, Coiffier B, Shipp MA, Fisher RI, *et al.*: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol 17:1244, 1999
- 12 Trotti A, Byhardt R, Stetz J, Gwede C, Corn B, *et al.*: Common toxicity criteria: version 2.0. an improved reference for grading the acute effects of cancer treatment: impact on radiotherapy. Int J Radiat Oncol Biol Phys 47:13-47, 2000
- 13 Kujawski LA, Longo WL, Williams EC, Turman NJ, Brandt N, *et al.*: A 5-drug regimen maximizing the dose of cyclophosphamide is effective therapy for adult Burkitt or Burkitt-like lymphomas. Cancer Invest 25:87-93, 2007
- 14 Lee EJ, Petroni GR, Schiffer CA, Freter CE, Johnson JL, *et al.*: Brief-duration high-intensity chemotherapy for patients with small noncleaved-cell lymphoma or FAB L3 acute lymphocytic leukemia: results of cancer and leukemia group B study 9251. J Clin Oncol 19:4014-4022, 2001
- 15 Thomas DA, Faderl S, O'Brien S, Bueso-Ramos C, Cortes J, *et al.*: Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer 106:1569-1580, 2006
- 16 Maruyama D, Watanabe T, Maeshima AM, Nomoto J, Taniguchi H, *et al.*: Modified cyclophosphamide, vincristine, doxorubicin, and methotrexate (CODOX-M)/ifosfamide, etoposide, and cytarabine (IVAC) therapy with or without rituximab in Japanese adult patients with Burkitt lymphoma (BL) and B cell lymphoma, unclassifiable, with features intermediate between diffuse large B cell lymphoma and BL. Int J Hematol 92:732-743, 2010