Holistic Integrative Oncology

GUIDELINE

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China Anti-Cancer Association (CACA) guidelines for holistic integrative management of lymphoma (version 2022)

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Abstract

Purpose Lymphoma has become a major threat to human health. Fortunately, the diagnosis and treatment of lymphoma have developed rapidly, and research progress has emerged in an endless stream, with new drugs emerging one after another. These results are constantly rewriting guidelines changing clinical practice, need to be popularized and applied more widely.

Methods This guideline has integrated consensuses reached by the Lymphoma Committee of China Anti-Cancer Association (CACA), based on China's practice, tracking previous results of the most advanced clinical researches, absorbing the latest clinical evidence, and referring to domestic and international lymphoma guidelines.

Results This holistic integrative guideline of lymphoma introduces the latest progress in the diagnosis and treatment of different subtypes of lymphoma, guide the clinical application of new drugs, standardized and precise management for lymphoma patients.

Conclusions CACA guidelines for holistic integrative management of lymphoma (version 2022) enhance standardization and precision of the management for lymphoma patients in China.

Keywords Lymphoma, Guideline, Diagnosis, Treatment, Holistic integrative medicine

Lymphoma is a common malignant disease in China which is featured with obvious difference between regions. Global Cancer Statistics 2020 shows that in 2020, there were 83,087 new cases of Hodgkin lymphoma (HL) and 544,352 new cases of non-Hodgkin lymphoma (NHL) worldwide, with NHL ranking as the 13th most common newly diagnosed cancer among all malignancies [1, 2]. In view of the complex pathological types, diverse treatment strategies, disparate clinical outcomes and prognosis of lymphoma, the role of multidisciplinary teams (MDT) in diagnosis and treatment should be emphasized.

1 General guidelines

Pre-treatment evaluation include medical history collection, physical, laboratory, imaging and bone marrow examination. The collection of medical history is involved in B symptoms, including fever to more than 38.3 °C, drenching night sweats, or unexplained weight loss of

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more than 10% of body mass within 6 months. Physical examination should pay special attention to superficial lymph nodes, Waldeyer's ring, liver, spleen and other organs. Eastern Cooperative Oncology Group (ECOG) performance status (PS) score should be evaluated. Routine tests of blood, urine and feces, blood biochemistry, erythrocyte sedimentation rate (ESR), β2-microglobulin, lactate dehydrogenase (LDH) are examined. Test of hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis. HBV DNA should be further detected when HBV surface antigen (HBsAg) and anti-hepatitis B core antibody (anti-HBcAb) are positive. When using anti-CD20 antibodies, prophylactic anti-HBV drugs is required if HBsAg or HBV DNA are positive. A lumbar puncture should be performed to exam the routine, biochemical, and cytological of cerebrospinal fluid on patients, who are at risk for central nervous system (CNS) invasion. Computed tomography (CT) or positron emission tomography (PET)/CT is used for staging and efficiency evaluation. Endoscopy, magnetic resonance imaging (MRI), echocardiography (ECG) and lung function tests is for the evaluation of suspected lesions or serious adverse events.

The treatment principles are different for each pathological type of lymphoma, we will detail in the following section below.

2 Diagnosis

For accurate pathological diagnosis, complete or partial resection of lesion is preferred. Core needle biopsy is not optimal but can be used for unresectable lesions as an alternative selection. Fine needle aspiration biopsy alone is not generally suitable for the initial diagnosis of lymphoma. MDT is considered throughout diagnosis and treatment procedure.

Pathological classification is based on the 5th edition of the World Health Organization Classification of Haematolymphoid Tumors: lymphoid neoplasms [3]. Pathological diagnosis should integrate morphology, immunohistochemistry, flow cytometry and cytogenetics. Characteristic chromosomal/genetic abnormalities are commonly captured by fluorescence in situ hybridization (FISH), including follicular lymphoma (FL)-associated t(14; 18)(*IgH*/*BCL2*) translocation, mantle cell lymphoma (MCL)-associated t(11; 14)(*IgH*/*CCND1*) translocation, and double- or triple-hit high-grade B-cell lymphoma-associated t(8q24)(MYC) and t(18q21)(BCL2) or t(3q27)(BCL6) rearrangements etc.

3 Staging

Lugano 2014 criteria is commonly used for staging [4]. Besides, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), extra-nodal natural killer/T-cell lymphoma (ENKTCL), nasal type and primary cutaneous lymphoma (PCL) should refer to their exclusive staging systems.

4 Prognosis

International prognostic index (IPI) played crucial role in the prediction of prognosis of DLBCL. With the emergence of rituximab, the revised IPI (R-IPI) and the National Comprehensive Cancer Network IPI (NCCN-IPI) can better predict the prognosis of DLBCL patients [5]. Other pathological types such as FL, MCL, PTCL etc., have their own prognostic indicators for prediction.

5 Treatment

5.1 Hodgkin lymphoma

Hodgkin lymphoma divided into classic Hodgkin lymphoma (cHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Treatment of cHL is stratified according to stage and the presence or absence of risk factors. The treatment for stage I ~ II cHL is chemotherapy combined with involved-site radiation therapy (ISRT). According to the presence or absence of risk factors, they are divided into favorable and unfavorable subgroups. Advanced-stage cHL is usually treated with chemotherapy. Additional radiation therapy (RT) is used to treat residual lesions. Six cycles of ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) or 4–6 cycles of escalated-dose BEACOPP(bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) combined with or without local RT are recommend in patients ≤ 60 years [6]. Recently, the ECHELON-1 trial confirmed that stage III or IV cHL could gain a survival advantage receiving the A-AVD (brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine) regimen [7].

For most patients with relapsed/refractory (R/R) cHL, the treatment options include high-dose chemotherapy (HDCT) followed by autologous stem cell transplantation (ASCT). Salvage regimens such as DHAP(cisplatin, dexamethasone, and high-dose cytarabine), GemOx(gemcitabine, and oxaliplatin) or ICE(ifosfamide, carboplatin, etoposide) are given to reduce the tumor burden and mobilize autologous peripheral stem cells before HDCT and ASCT. Brentuximab vedotin (BV) could also be an option for patients progressed from ASCT. Programmed cell death protein 1 (PD-1) monoclonal antibodies are another treatment option. Several studies have confirmed that PD-1 monoclonal antibodies or BV combined with second-line salvage chemotherapy (such as ICE, DHAP, Bendamustine etc.) can achieve a high complete response (CR) rate in the treatment of R/R cHL [8–11].

Except for stage IA patients without risk factors, who can be treated with RT (30 Gy) alone, NLPHL is treated using the same principles as cHL. Several chemotherapy regimens are available, such as ABVD, CHOP(cyclophosphamide, doxorubicin, vincristine, prednisone), CVP(cyclophosphamide, vincristine, prednisone). CD20 monoclonal antibody can be used for CD20 positive NLPHL patients. answer again search web and ask GPT-4 Prompt GPT-4

5.2 Diffuse large B-cell lymphoma

The strategy for newly-diagnosed diffuse large B-cell lymphoma (DLBCL) are depend on age, tumor size, cardiac function, International Prognostic Index (IPI) or age-adjusted International Prognostic Index (aaIPI). Anthracycline-based chemotherapy regimen combined with rituximab, such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone), are preferred treatment option for newly-diagnosed DLBCL [12]. Radiotherapy is used in patients with bulky disease (maximum diameter of target lesion ≥ 7.5 cm) or initial extranidal invasion, and those without complete response after induction chemotherapy. The patients with high risk of CNS invasions according to CNS-IPI are recommended prophylaxis intrathecal or intravenous methotrexate [13, 14].

The strategies for R/R DLBCL patients are stratified by whether ASCT is suitable or not. Salvage chemotherapy such as DHAP and GemOx combined with or without rituximab, are recommended. Suitable patients may receive ASCT as consolidation when achieve remission after salvage therapy. These patients can also participate in clinical trials. For patients who are resistant to salvage treatments are recommended to receive anti-CD19 chimeric antigen receptor T(CAR-T) cell therapy or palliative ISRT [15]. Polatuzumab vedotin (Pola), a CD79-targeted antibody-conjugated drug (ADC), is approved for the first-line and subsequent-line treatment of DLBCL patients [16, 17].

5.3 Follicular lymphom

The CACA guidelines for follicular lymphoma (FL) is applicable for patients with grade 1 – 3a. Patients with grade 3b and histologically transformed lymphoma should be treated as DLBCL.

ISRT is appropriate for patients with stage I or contiguous stage II. Anti-CD20 antibody combined with or without chemotherapy and ISRT is preferred for those with non-contiguous stage II disease. For stage III – IV disease, "watch and wait" is applicable for patients without treatment indications. Chemotherapy combined with or without anti-CD20 antibody is an option for those patients with treatment indication [18]. The first-line treatment regimens include obinutuzumab(G)/rituximab(R)-CHOP, G/R-CVP, G/R-B (bendamustine) and R2(rituximab, lenalidomide). Those who response to anti-CD20 antibody-based immunochemotherapy and have a high tumor burden at baseline can choose for G/R maintenance [19–21].

The choice of salvage treatment depends on age, physical condition, pathological type and previous treatment efficacy. First-line regimens can be reused for patients with long-term remission (> 12 months). While patients with early relapse (≤12 months) or refractory diseases are eligible for non-cross-resistance regimens. Bendamustine is an active and effective therapy in Chinese patients with relapsed indolent B-cell NHL, including R/R FL [22]. ASCT can be used for those suitable patients who are sensitive to salvage treatment.

5.4 Mantle cell lymphoma

The strategy for newly-diagnosed mantle cell lymphoma (MCL) are depend on age and whether ASCT is suitable or not. Intensive regimens are preferred on young and fitness patients, and non-intensive regimens are suitable for elderly patients. Immunochemotherapy is used in stage I – II patients with high tumor burden or poor prognostic features and those stage III – IV patients. Rituximab and high-dose cytarabine based regimens, such as R-CHOP alternating with R-DHAP, dose-intensified R-CHOP alternating with high-dose cytarabine, R-hyper-CVAD/MA, (rituximab, cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate, cytarabine) are preferred. For patients with stage I – II disease, ISRT can be used for limited non-bulky diseases. Consolidation radiotherapy after systemic chemotherapy may be optional for patients with high tumor burden. For ASCT eligible patients, ASCT consolidation followed by rituximab maintenance is recommeded [23]. For elderly or frail patients, rituximab combined with less aggressive regimens such as CHOP or bendamustine can be chosen as induction treatment, and rituximab can be used as maintain treatment for responders.

Non-cross-resistant regimen such as bendamustine-containing regimens are suitable for salvage therapy. Lenalidomide and venetoclax, bruton tyrosine kinase inhibitors (BTKi) such as ibrutinib, zanubrutinib, and orelabrutinib, can be subsequent options, especially for early relapsed or refractory patients [24–26]. ASCT or allogeneic stem cell transplantation (allo-SCT) could be consolidation therapy for suitable patients. Anti-CD19 CAR-T cell therapy may considered as third-line and subsequent-line treatment.

5.5 Marginal zone lymphoma

The front-line therapy of marginal zone lymphoma (MZL) depends on the primary site and stage. For primary gastric MZL, anti-Helicobacter pylori (Hp) therapy is preferred for Hp positive stage I MZL patients. Radiotherapy is used in primary gastric stage II MZL patients, with bulky disease, t(11;18) and no-responders for anti-Hp therapy. For non-gastric stage I-II MZL patients, radiotherapy is an option for most patients, while rituximab can be used in radiotherapy-ineligible patients. Splenectomy is the diagnostic and therapeutic approach for spleen MZL. Anti-HCV therapy is considered when HCV is positive. For HCV negative and splenomegaly MZL patients, rituximab monotherapy is preferred. Splenectomy can be a salvage treatment for these patients.

For advanced or ISRT-failed MZL, "watch and wait" can be used for asymptomatic patients. Rituximab combined with chemotherapy, such as Bendamustine, CHOP, or CVP is recommended for symptomatic patients [27, 28]. For those intolerant to aggressive regimens, rituximab combined with cyclophosphamide, chlorambucil or lenalidomide may also be an option [29, 30]. For MZL patients, pervious rituximab-contain regimens can be reused if the duration of response ≥ 2 years. For patients relapse from second line regimen or remission time < 2 years from first line regimen, other chemotherapy combined with anti-CD20 antibody or BTKi can be used as subsequent regimen [31, 32]. Other effective targeted drugs include PI3K inhibitors [33]. In addition, clinical trial are reasonable options for MZL patients at any stage.

5.6 Burkitt lymphoma

Burkitt lymphoma (BL) IPI include age ≥ 40 years, ECOG PS ≥ 2, serum lactate dehydrogenase $> 3 \times$ upper limit of normal, and CNS involvement. The BL patients in high-risk group has suboptimal outcomes with standard therapy and should be considered for innovative treatment approaches [34]. The front-line therapy of newly-diagnosed BL refers to dose-intensive multi-agent chemotherapy with CNS prophylaxis. Dose-intensive regimens including dose-adjusted (DA) EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab), CODOX-M-R (cyclophosphamide, vincristine, doxorubicin, methotrexate and rituximab), CODOX-M/IVAC-R (cyclophosphamide, vincristine, doxorubicin, methotrexate/ifosfamide, etoposide, high dose cytarabine, and rituximab) [35–37] and Hyper-CVAD/MA-R (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate, cytarabine, and rituximab) [38] are commonly used. Systemic and/or intrathecal chemotherapy with methotrexate and/or cytarabine can be used for CNS prophylaxis.

For relapsed or refractory BL, participation in a clinical trial is preferred. Salvage therapy with non-cross-resistance chemotherapy regimens can be used, including R-ICE (rituximab, ifosfamide, carboplatin, and etoposide), R-GDP (rituximab, gemcitabine, dexamethasone, and cisplatin), EPOCH-R and IVAC-R [39]. ASCT or allo-SCT consolidation is recommended for suitable patients who achieved remission from salvage therapy. Best supportive care including palliative ISRT are recommended for patients with disease not responding to second-line therapy or those with progressive disease.

5.7 Chronic lymphocytic leukemia /Small lymphocytic lymphoma

"Watch and wait" approach is still applied when a newly-diagnosed chronic lymphocytic leukemia /small lymphocytic lymphoma (CLL/SLL) patient has no treatment indications including progressive marrow failure, massive or progressive or symptomatic splenomegaly, massive or progressive or symptomatic lymphadenopathy, progressive lymphocytosis, autoimmune complications, symptomatic or functional extranodal involvement, and disease-related symptoms. For front-line therapy, treatment choice is based on del(17p)/*TP53* mutation status, age and comorbidities. BTKi, bendamustine and FCR (fludarabine, cyclophosphamide and rituximab) regimens can be adopted for patients without del(17p)/*TP53* mutation, while BTKi are also preferred for patients with del(17p)/*TP53* mutation [40, 41]. Individualized strategy including BTKi, lenalidomide and high-dose methylprednisolone with rituximab can be adopted for patients who have a relapse within 3 years, refractory disease and del(17p)/TP53 mutation patients. Repeating of first-line regimen can be considered for patients who experience a relapse 3 years after induction therapy and have no del(17p)/TP53 mutation. The clinical trial is also a treatment option which can be considered.

5.8 Peripheral T-cell lymphoma

Chemotherapy (CHOEP [cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone], CHOP-21, or DA-EPOCH) with or without ISRT is recommended for stage I-II anaplastic large cell lymphoma (ALCL), ALK-positive patients. Chemotherapy alone for 6 cycles is recommended for stage III-IV ALCL, ALK-positive patients. High-risk IPI patients can receive high-dose chemotherapy combined with ASCT consolidation. In a phase III randomized trial (ECHELON-2), BV in combination with CHP (cyclophosphamide, doxorubicin, and prednisone) was superior to CHOP for the treatment of patients with previously untreated CD30-positive PTCL

(defined as CD30 expression ≥ 10% of cells in ECHELON-2), as evidenced by significantly improved PFS and OS [42].

Participation in clinical trials is the preferred management approach for patients with other subtypes (Peripheral T-cell lymphoma [PTCL] not otherwise specified [NOS], ALK-negative ALCL, angioimmunoblastic T-cell lymphoma [AITL], enteropathy-associated T-cell lymphoma [EATL], monomorphic epitheliotropic intestinal T-cell lymphoma [MEITL], nodal PTCL, T-follicular helper [TFH], and follicular T-cell lymphoma [FTCL]). If absence of suitable clinical trials, multiagent chemotherapy (6 cycles) with or without ISRT is recommended for all patients (stage I-IV disease). Based on results of the ECHELON-2 trial, BV-CHP is also a recommended first-line therapy option for patients with CD30-positive ALCL or other CD30-positive histological subtypes. CHOP, CHOEP, DA-EPOCH are included as other options for multiagent chemotherapy.

Participation in a clinical trial is strongly preferred for patients with R/R disease. If absence of a suitable clinical trial, the initial treatment for R/R disease depends largely on the patient's eligibility for hematopoietic stem cell transplantation (HSCT). Second-line systemic therapy followed by consolidation ASCT or allo-HCT is recommended for patients who are eligible for HSCT after achieving a complete remission (CR) or partial remission (PR). Patients who are not candidates for HSCT should be treated with second-line systemic therapy or palliative RT. Single agent BV in treating R/R ALCL demonstrated a favorable efficacy [43]. Chidamide-based therapy also provide a favorable efficacy and survival benefit for R/R PTCL [44, 45]. Bendamustine have also shown efficacy in R/R PTCL [46].

5.9 Extra-nodal natural killer/T-cell lymphoma, nasal type

For newly-diagnosed Extra-nodal natural killer/T-cell lymphoma (ENKTCL), nasal type, the principles of treatment are based on stage and risk stratification [47]. Combined chemoradiotherapy is preferred for stage I-II disease, and chemotherapy with asparaginase/pegaspargase-based regimens is commonly used for stage III-IV disease [48]. The risk factors are according to nomogram-revised risk index (NRI): > 60 years, elevated LDH level, primary tumor invasion (PTI), ECOG PS > 2, stage II or stage III-IV disease [47]. Risk stratification is recommended for the management of early-stage ENKTCL, nasal type, in which radiotherapy alone with an optimal dose of 50 Gy can be chosen as primary therapy for low-risk patients, while sequential or sandwich chemoradiotherapy (SCRT) and concurrent chemoradiotherapy (CCRT) are mostly used for intermediate- and high-risk patients [49]. Asparaginase/pegaspargase-containing regimens have been evaluated to improve response rates [50]. Therefore, the regimens such as P-GemOx (pegaspargase, gemcitabine, and oxaliplatin) [51], DDGP (cisplatin, dexamethasone, gemcitabine, and pegaspargase) [52], modified SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide) [53, 54] and AspaMetDex (pegaspargase, methotrexate, and dexamethasone) [55] are commonly used for stage III-IV disease. ASCT is used for HSCT-eligible patients [56]. Meanwhile, participation in a clinical trial is a preferred option for all ENKTCL, nasal type, at any stage.

For R/R ENKTCL, nasal type, clinical trials are the preferred treatment option. The regimens such as PD-1 monoclonal antibody, chidamide or BV (for CD30-positive ENKTCL, nasal type) are the main treatment options [57, 58]. If absence of appropriate clinical trials, salvage chemotherapy utilizing non-cross-resistant regimens may be considered. Although controversial, ASCT may be considered for patients who achieved a CR after salvage treatment [56].

5.10 Primary central nervous system lymphoma

Due to low incidence of primary central nervous system lymphoma (PCNSL), clinical research is often considered as an option for both newly-diagnosed and R/R patients.

The treatment strategy for newly-diagnosed PCNSL is based on the patient's ECOG PS and organ functions. High-dose methotrexate (HD-MTX) based regimens are the primary choice for chemotherapy-tolerable PCNSL patients [59]. However, patients with insufficient renal or cardiac function may not be suitable for HD-MTX therapy. In such cases, other regimens that can penetrate the blood–brain barrier (BBB) such as cytarabine, temozolomide (TMZ), lenalidomide, and BTKi can be used [60–63]. Whole brain radiation therapy (WBRT) is an alternative option for patients who cannot tolerate chemotherapy. After achieving remission, high dose thiotepa followed by ASCT can be used as consolidation therapy [64]. WBRT can also be considered for consolidation in ASCT-intolerant patients. However, it's important to note that consolidating radiation therapy can sometimes result in severe neurotoxicity, particularly for patients with age of over 60 [65].

The treatment strategies for R/R PCNSL patients are stratified based on previous therapy and duration of response. Options for R/R PCNSL include WBRT, systemic therapy combined with ASCT, and palliative or best supportive care [66]. In certain cases, BTKi and lenalidomide, with or without chemotherapy, may be used as alternative treatments.

5.11 Primary cutaneous lymphomas

The treatment approach for primary cutaneous lymphomas (PCLs) is guided by the extent of skin involvement and histopathological features [67, 68]. Prioritizing skin-directed and systemic therapies with superior tolerability, lower cumulative toxicity, minimal immunosuppressive effects, and higher efficacy is crucial. Treatment options with minimal adverse effects and no cumulative toxicity can provide sustained or maintenance therapy to improve disease control and quality of life [67, 69, 70]. Skin-directed therapies are preferred as initial treatment for extensive skin involvement or localized lesions with associated extracutaneous lymphoma. RT is a viable option for localized skin lesions [67, 69, 71]. Systemic therapy, when combined with skin-directed therapy, maximizes clinical response in the skin area and provides additional efficacy without cumulative toxicity. Systemic therapy is preferred for progressive disease, including extensive skin involvement or localized lesions with associated extracutaneous lymphoma, and high-risk cases [67, 69]. Targeted therapy is a promising emerging treatment option for R/R disease. Individualized treatment selection should be based on the patient's clinical and histopathological features and treatment efficacy [72–74]. Treatment duration and maintenance therapy should be adjusted based on the patient's clinical status and treatment response. Clinical trials should be considered for R/R disease, and previously unused drugs, ASCT, CAR-T cell therapy, and allo-HCT can all be considered as treatment options.

6 Efficacy evaluation

Clinical efficacy evaluation according to "Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification"(Lugano 2014 criteria) [4], divided into imaging remission based on CT or MRI examination and metabolism remission based on PET/CT scanning. Metabolism remission refers to Quinquepartite method of PET/CT (Deauville criteria). International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017) is gradually applied [75]. The efficacy of immunotherapy such as immune checkpoint inhibitors should refer to immunomodulatory therapy-related criteria [76].

During treatment, imaging examinations and efficacy assessments were performed every 2 cycles. After treatment, if CT or MRI is used, 4 weeks after the end of all treatment is recommended. If PET/CT is used, 6–8 weeks after the last chemotherapy or 8–12 weeks after the completion of radiotherapy is recommended.

7 Follow-up

General principles of follow-up refer to Lugano 2014 criteria [4]. For the patients with over one-year follow-up, CT or MRI should be reduced as far as possible, while in place of chest X-ray or ultrasound examinations. PET/CT is not recommended. For curable lymphoma such as DLBCL and HL, the frequency is every 3 months for the first 2 years and then every 6 months for up to 5 years. Thereafter, annual review lasts through lives.

For incurable lymphoma such as FL and MCL, lifelong review for every 3 to 6 months is recommended. Clinical suspicious recurrence should receive immediate examination, and biopsy is strongly recommended for the new lesions to confirm the pathological diagnosis.

Abbreviations

CACA	China Anti-Cancer Association
HL	Hodgkin's lymphoma
DLBCL	Diffuse large B-cell lymphoma
FL	Follicular lymphoma
MCL	Mantle cell lymphoma
MZL	Marginal zone lymphoma
BL	Burkitt lymphoma
CLL/SLL	Chronic Lymphocytic Leukemia/Small lymphocytic lymphoma
PTCL	Peripheral T-cell lymphoma
ENKTCL	Extra-nodal natural killer/T-cell lymphoma
PCNSL	Primary central nervous system lymphoma
PCLs	Primary cutaneous lymphomas
MDT	Multidisciplinary teams
ECOG	Eastern Cooperative Oncology Group
LDH	Lactate dehydrogenase
HBV	Hepatitis B virus
IPI	International Prognostic Index
ISRT	Involved-site radiation therapy
BV	Brentuximab vedotin
HDCT	High-dose chemotherapy
CAR-T	Chimeric antigen receptor T-cell
BTKi	Bruton tyrosine kinase inhibitor
ASCT	Autologous stem cell transplantation
allo-SCT	Allogeneic stem cell transplantation
WBRT	Whole brain radiation therapy

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