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PROGRESS IN HEMATOLOGY

Current status and progress of lymphoma research in East Asian countries

Lymphoma epidemiology in Korea and the real clinical field including the Consortium for Improving Survival of Lymphoma (CISL) trial

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Abstract
Lymphomas are a heterogeneous group of disease entities with well-defined clinical, morphological, immunophenotypic, and cytogenetic characteristics. Moreover, regional and racial differences have been reported in their incidence and subtype compositions. Here, we reviewed the epidemiology of lymphomas and summarized the recent achievements in specific subtypes prevalent in Korean population, focusing on clinical studies conducted by the Consortium for Improving Survival of Lymphoma (CISL) of the Korean Society of Hematology Lymphoma Working Party (KSH-LWP).

Keywords Lymphoma · Korea · Epidemiology · Clinical trial

Introduction

Lymphomas are the most common hematologic malignancies and a heterogenous group of neoplasms with diverse clinical presentations and histological and biological features. They originate from neoplastic clones of B, T, or natural killer (NK) cells and are classified based on clinical, morphological, immunophenotypic, and cytogenetic characteristics [1]. The classification of lymphoid neoplasms was derived from the Revised European–American Classification of Lymphoid Neoplasms (REAL) published by the International Lymphoma Study Group in 1994 [2] and the World Health Organization classification (WHO) of lymphoid neoplasms first published in 2001 and revised in 2008 and 2016 [3, 4].

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As diagnoses and classification systems for lymphoid neoplasms have been established, there have been efforts to investigate and report the epidemiology of lymphomas. Likewise, the Korea Central Cancer Registry (KCCR) and the Korean Society of Hematology (KSH) jointly investigated the domestic prevalence and incidence rates of hematologic malignancies since 1999 and analyzed survival rates of patients [5, 6]. Different incidence rates and trends have been reported for specific subtypes of lymphomas among regions, and some discriminative features were reported in the Asian population in the United States or Europe [7]. For example, decreased incidence rate in the Asian population for overall lymphoid malignancies was observed, which was prominent for follicular lymphoma (FL), chronic lymphocytic leukemia (CLL), and Hodgkin lymphoma (HL). However, Asians showed an increased incidence rate of the marginal zone lymphoma (MZL) and extranodal NK/T-cell lymphoma (ENKTL), nasal type [8–10].

In this article, we comprehensively reviewed the incidence, distribution, and survival rates of lymphoid neoplasms in Korean population based on the KCCR data. Furthermore, we summarized recent advances in diagnostic and therapeutic approaches focusing on clinical trials conducted by the Consortium for Improving Survival of Lymphoma (CISL) of the Korean Society of Hematology Lymphoma Working Party (KSH-LWP).

Korean lymphoma epidemiology

Cancer registration in Korea

In 1980, the Korean Ministry of Health and Welfare initiated the KCCR, a nationwide hospital-based cancer registry for collecting data from 47 hospitals in Korea, and became the entire population-based cancer registry program in 1999. KCCR subsequently published annual reports on cancer statistics in Korea, and the latest 2014 version was issued in October 2016. Initially, cancer diagnosis was classified according to the International Classification of Diseases for Oncology 3rd edition (ICD-O-3), which was converted to the International Classification of Diseases 10th edition (ICD-10). Incidence data from 1999 to 2012 were obtained from the Korea National Cancer Incidence Database (KNCI DB). The completeness of incidence data in 2012 was 97.7%, as determined by the Ajiki method [11].

Incidence of lymphoid neoplasms and subtypes between 1999 and 2012

Lee et al. reported the subtype-specific statistical analysis of lymphoid malignancies in the Korean population in 2017, based on the KCCR annual report data between 1999 and 2012 [12]. This article contained the most recent data regarding the details of each subtype in lymphoid neoplasms, and the authors comprehensively analyzed the incidences and changes of survival rates over 20 years. We summarized Korean lymphoma epidemiology mainly based on the results in this article and the annual report of cancer statistics in Korea. Between 1999 and 2012, a total of 65,948 cases of lymphoid neoplasms occurred, which comprised 3.0% of all cancers reported. Based on subtypes, mature B-cell neoplasms (42,647 cases, 64.7%) were the most common, followed by precursor cell neoplasms (7409 cases, 11.2%), unknown types (6618 cases, 10.0%), and mature T- and NK-cell neoplasms (6612 cases, 10.0%) (Fig. 1a). Eleven cases of composite Hodgkin and non-Hodgkin lymphoma were not included (Fig. 1). Among the mature B-cell neoplasms excluding plasma cell disorders (11,169 cases, 26.2% of mature B-cell neoplasms), diffuse large B-cell lymphoma (DLBCL; 19,659 cases, 62.5%) was the most common subtype, followed by MZL (6716 cases, 21.3%) (Fig. 1b). The incidences of follicular lymphoma (FL; 1498 cases, 4.8%) and chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL; 1495 cases, 4.7%) were relatively lower than those in the Western population [13, 14]. Among the mature T- and NK-cell neoplasms, peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS; 2157 cases, 32.6%), was the most common, followed by ENKTL (1846 cases, 27.9%), angioimmunoblastic T-cell lymphoma (AITL; 831 cases, 12.6%), anaplastic large-cell lymphoma (ALCL; 786 cases, 11.9%), and cutaneous T-cell lymphoma (CTCL; 744 cases, 11.3%) (Fig. 1c). Similar to other Asian countries, the incidence of ENKTL was higher than that in the Western countries [15, 16].

Annual changes on the incidence based on subtypes and age group

Figure 2 presents the annual incidences of all lymphoid neoplasms and each subtype between 1999 and 2012. In 1999, 3233 cases of lymphoid neoplasms were reported to the registry. In 2012, a total of 6638 cases of lymphoid neoplasms were reported, including 4844 cases of mature B-cell neoplasms and 634 cases of T- and NK-cell neoplasms. During this period, the crude incident rate (CR) and age-standardized incidence rate (ASR) of all lymphoid neoplasms increased from 6.85 to 13.18 and 6.89 to 9.93, respectively. Furthermore, the annual percentage change (APC) of ASR was 3.2%, with statistical significance of $p < 0.05$). Between 1999 and 2012, the ASRs of mature B-cell neoplasms and mature T- and NK-cell neoplasms increased from 3.41 to 6.60 (APC 5.6%) and from 0.47 to 0.95 (APC 6.6%), respectively. Moreover, ASR increased from 0.24 to 0.46 in HL (APC 5.0%) and from 1.33 to 1.50 in precursor cell neoplasms (APC 1.4%). However, ASR of unknown types decreased from 1.44 to 0.41 (APC − 9.3%).

Figure 3 presents the incidences based on age group in 2012. A high incidence of lymphoid neoplasms was observed in the group aged 50–79 years. Mature B-cell neoplasms were the most prevalent subtype in all groups aged ≥ 20 years. However, precursor cell neoplasms were the most common subtype in patients aged < 20. The peak incidence of HL was observed at between 20 and 29 years of age, which was different from the bimodal distribution observed in the Western population. The unknown type of lymphoid neoplasm was relatively rare in the younger patient group.

Survival changes based on time in major subtypes

The KCCR has been collecting survival data of patients with cancer since their first diagnosis in 1993. Lee et al. analyzed the survival rates of patients with lymphoid neoplasms based on the data available in the KNCI DB between 1993 and 2012 [12]. Patients with lymphoid neoplasms were divided by 5-year intervals (1993–1997, 1998–2002, 2003–2007, and 2008–2012) and major subtypes such as HL, DLBCL, PTCL, and ENKTL. The 5-year relative survival rate (5-RSR) of all lymphoid neoplasms between 1993

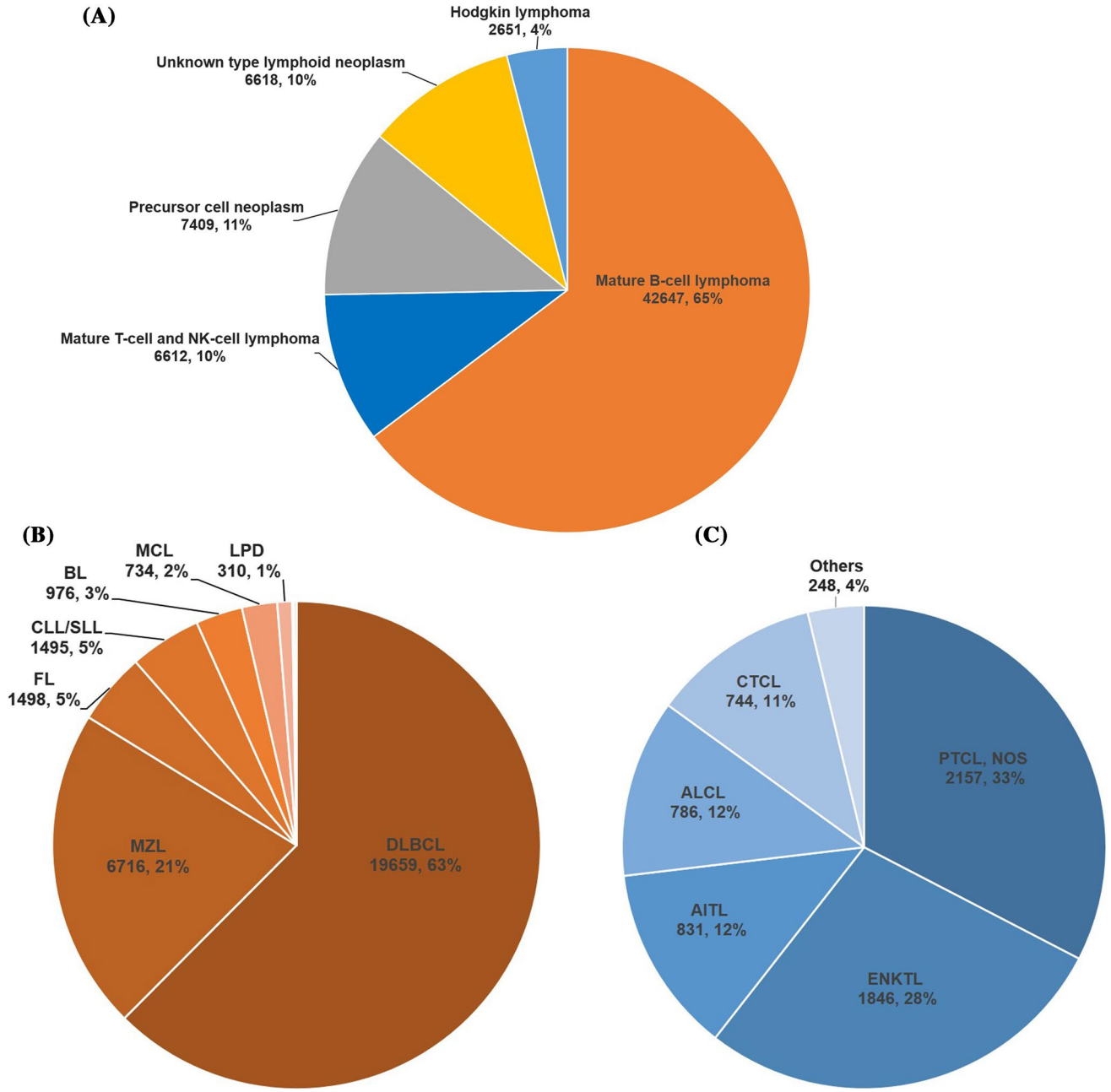
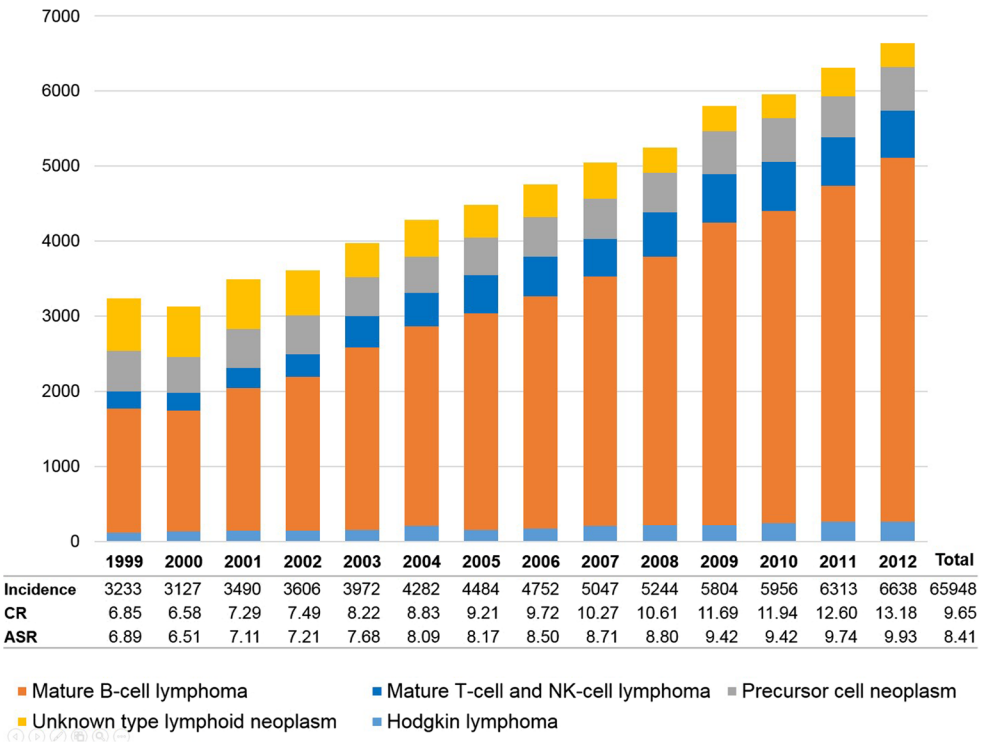


Fig. 1 Incident cases of the **a** entire lymphoid neoplasms, **b** mature B-cell lymphoma, and **c** mature T- and NK-cell lymphoma between 1999 and 2012. **b** *DLBCL* diffuse large B-cell lymphoma, *MZL* marginal zone lymphoma, *FL* follicular lymphoma, *CLL/SLL* chronic lymphocytic leukemia/small lymphocytic leukemia, *BL* Burkitt lymphoma, *MCL* mantle cell lymphoma, *LDP* lymphoproliferative disorder. **c** *PTCL-NOS* peripheral T-cell lymphoma, not otherwise specified, *ENKTL* extranodal NK/T-cell lymphoma, *AITL* angioimmunoblastic T-cell lymphoma, *ALCL* anaplastic large-cell lymphoma, *CTCL* cutaneous T-cell lymphoma

and 1997 was 45.3%, which gradually increased to 61.7% in 2008–2012. The 5-RSR improved in most subtypes of lymphoid neoplasms. The HL showed the most favorable 5-RSR, from 71.1% in 1993–1997 to 83.0% in 2008–2012. The 5-RSR of mature B-cell neoplasms improved from 42.8 to 63.8%, with the greatest improvement observed between 1998–2002 and 2003–2007 (47.9 and 58.7%). This increment (10.8%) is consistent with the results of survival in DLBCL, comparing the pre- and post-rituximab eras in the United States [17]. For similar reason, survival rates for FL also increased in this period. However, the survival rates for T- and NK-cell neoplasms, except CTCL, did not improve during this period (5-RSR, 44.2% to 44.2% between 1993–1997 and 2008–2012, respectively). The 5-RSR of



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Incidence	3233	3127	3490	3606	3972	4282	4484	4752	5047	5244	5804	5956	6313	6638	65948
CR	6.85	6.58	7.29	7.49	8.22	8.83	9.21	9.72	10.27	10.61	11.69	11.94	12.60	13.18	9.65
ASR	6.89	6.51	7.11	7.21	7.68	8.09	8.17	8.50	8.71	8.80	9.42	9.42	9.74	9.93	8.41

Fig. 2 Annual changes in the incidence based on the subtypes of lymphoid neoplasms, 1999–2012. *CR* crude incident rate, *ASR* age-standardized incidence rate

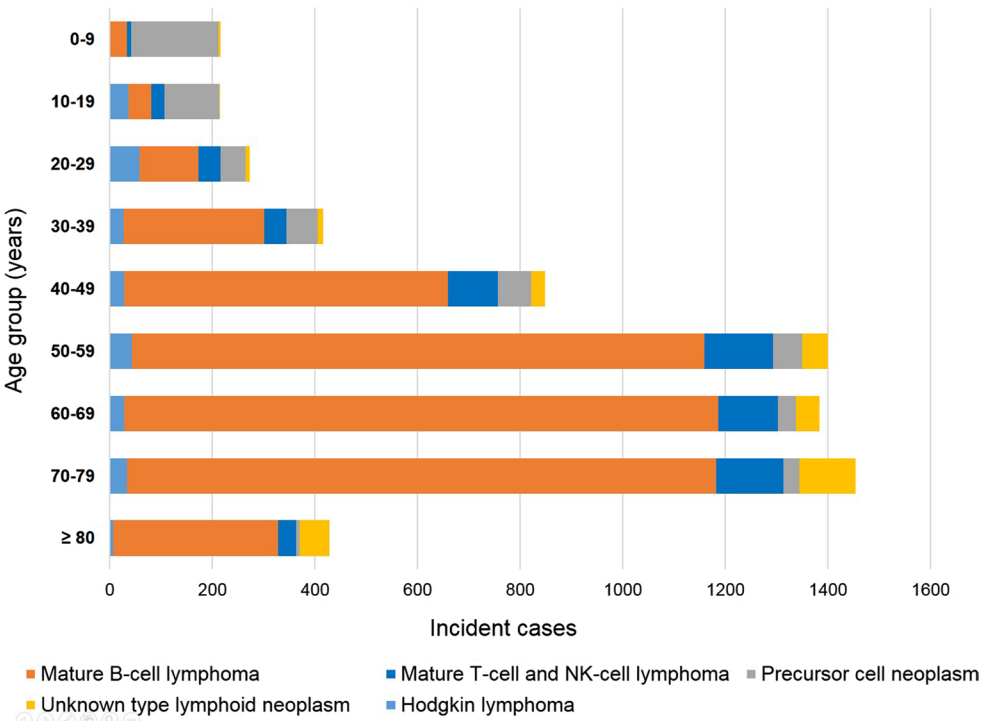


Fig. 3 Incident cases by age group, 2012

ENKTL improved from 45.8% in 2003–2007 to 49.9% in 2008–2012, because concomitant or sequential chemotherapy and radiation therapy became the standard treatment in early stages of ENKTL [18, 19], and L-asparaginase-based regimens were introduced for advanced diseases [20, 21]. However, most subtypes of T-cell lymphoma were under unsatisfactory situations with lack of successful trials on new drug combinations. The survival rates for acute lymphoblastic leukemia/lymphoma also significantly improved with 56.3% of 5-RSR in 2008–2012.

Recent advances in Korean lymphoma focusing on CISL trials

CISL

CISL of KSH-LWP is a multicenter collaborative study group for patients with lymphoma [22]. The first meeting was held in February 2006, with 10 institutions and 12 members and, currently, the CISL comprises 69 centers. By the end of 2017, the CISL has published the results of 36 retrospective studies to investigate the clinical and pathological features of Korean-specific lymphoma subtypes and evaluate the outcomes of new therapeutic modalities. Moreover, they also have performed more than 35 prospective clinical trials and reported the results of 20 prospective trials for DLBCL, MZL, ENKTL, and other subtypes [23]. Figure 4 presents the prospective chronological flow of prospective CISL trials.

HL

CISL evaluated the clinical and histopathological characteristics, therapeutic outcomes, and prognostic factors of Korean patients with HL [24]. A total of 539 patients with HL from 16 centers were retrospectively analyzed between 1985 and 2010. This study revealed lower incidence of HL in Korea than in Western countries and similar distribution of morphologic subtypes and treatment outcomes. The median age of all patients was 40 years, and the peak incidence was found in the group aged 16–30 years. Among the 539 patients, 506 (93.9%) had classical HL and 267 (48.7%) had advanced stages (Ann Arbor stage III or IV) at the time of initial diagnosis.

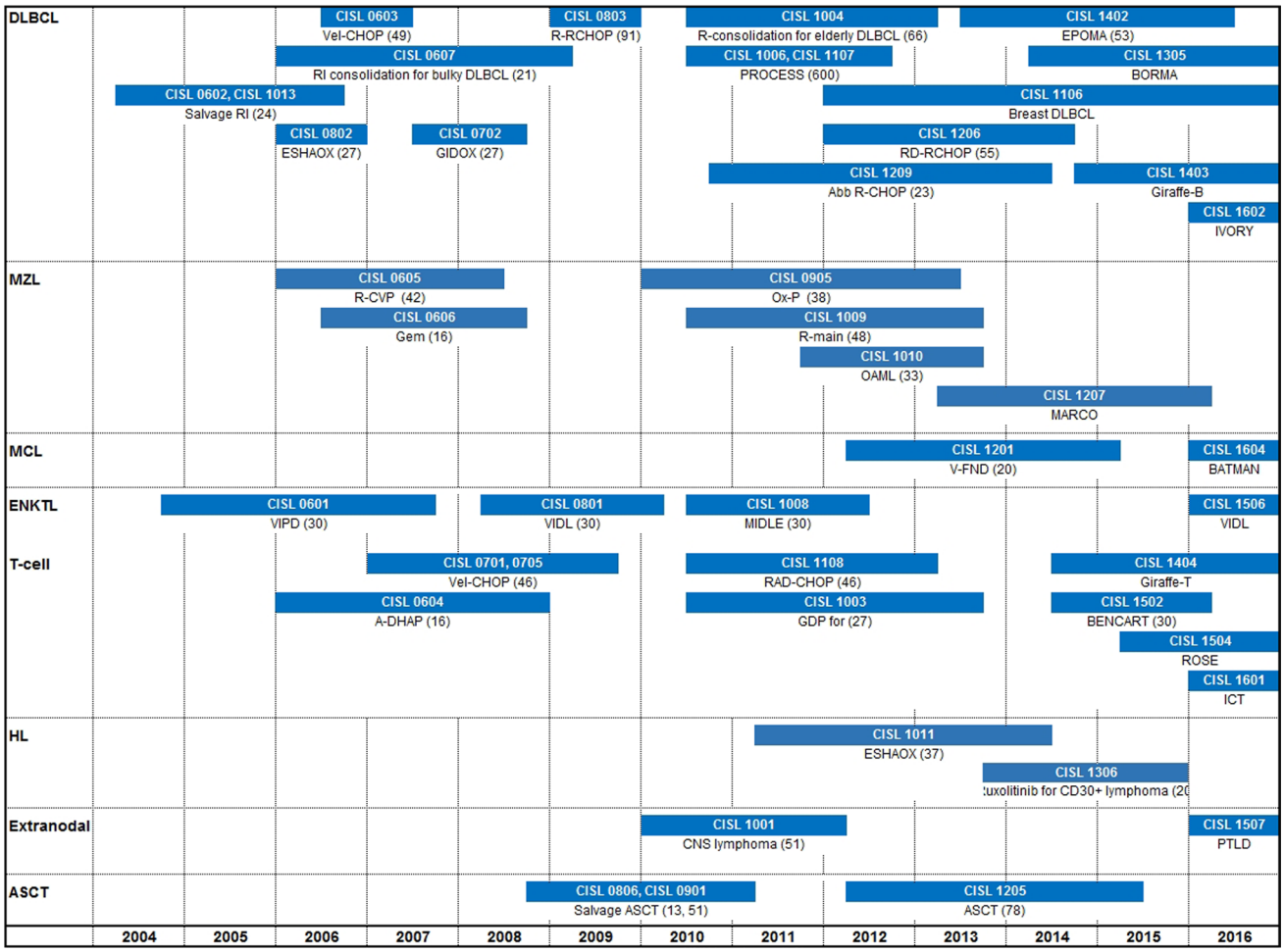


Fig. 4 Chronological flow of prospective trials in Consortium for Improving Survival of Lymphoma (CISL). *DLBCL* diffuse large B-cell lymphoma, *MZL* marginal zone lymphoma, *MCL* mantle cell lymphoma, *ENKTL* extranodal NK/T-cell lymphoma, *HL* Hogkin lymphoma, *ASCT* autologous hematopoietic stem cell transplantation

B-cell neoplasms

DLBCL

To retrospectively analyze DLBCL, CISL has focused on the diseases in the extranodal primary sites, such as the breast, ovary, intestine, adrenal gland, and sinonasal tract. A retrospective analysis of primary breast DLBCL reported different treatment outcomes, prognoses, and progression patterns between patients with only one extranodal disease in the breast and multiple sites of extranodal disease [25]. Moreover, a matched-pair analysis comparing the outcomes of primary breast and nodal DLBCL was also performed. Overall survival (OS) was similar between the two groups in rituximab era; however, extranodal progression in the breast or central nervous system (CNS) was more common in the primary breast DLBCL than in the nodal DLBCL [26]. Outside the CISL group, a single-center analysis emphasized the number of extranodal sites involved as the most significant prognostic factor for event-free survival (EFS) and OS in R-CHOP-treated patients with disseminated DLBCL [27]. The CISL also conducted a retrospective cohort study to analyze the effect of surgery on the outcomes and quality of life (QoL) in the intestinal DLBCL [28]. This study showed that surgical resection followed by chemotherapy is an effective treatment strategy with acceptable QoL deterioration for localized intestinal DLBCL. The CISL also reported the prognostic factors in primary DLBCL of adrenal gland, and suggested that achieving complete response (CR) after R-CHOP is predictive survival [29]. Recently, primary sinusoidal tract DLBCL treated with R-CHOP was retrospectively investigated. The results suggested that introduction of rituximab improved the OS and reduced CNS relapse in patients with sinusoidal tract DLBCL [30]. Moreover, the CISL analyzed 1585 DLBCL patients with bone marrow (BM) aspirates at diagnosis. Histologic BM involvement and chromosomal abnormalities were found in 259 (16.3%) and 192 (12.1%) patients, respectively. We subsequently reported that multiple cytogenetic abnormalities in the BM were associated with poor prognosis. [31].

For the prospective study in DLBCL, the CISL started a phase I/II study of bortezomib plus CHOP every 2 weeks (Vel-CHOP-14) in patients with advanced stage of DLBCL in 2006 (CISL 0603). In phase II, the overall response rate (ORR) was 95% [CR 80%; partial response (PR) 15%]. However, 9 out of 40 patients (22.5%) showed grade 3/4 sensory neuropathy, and 22 (55.0%) required at least 1 dose reduction. We concluded that Vel-CHOP-14 was highly effective for the treatment of untreated DLBCL; however, dose or schedule modification was required to reduce neurotoxicity [32]. Since 2010, the CISL has tried weekly rituximab (R) consolidation following four cycles of R-CHOP in elderly ($\geq$ 70 years) patients (CISL 1006). We showed an acceptable response with high tolerability of R consolidation, with 78.4% of ORR, 63.9% of 2-year PFS, and 68.7% of 2-year OS [33]. Most recently, the CISL conducted a prospective cohort study with risk-adapted CNS evaluation in DLBCL (CISL 1006, 1107). We analyzed 595 patients with DLBCL who received R-CHOP and revealed that highly elevated serum lactate dehydrogenase (LDH, more than 3 times the upper limit of the normal range) is an independent prognostic factor for CNS relapse [34].

Another mainstream of clinical trials in CISL targeting DLBCL was radioimmunotherapy (RIT). First, radioiodinated rituximab (^{131}I-rituximab) was attempted in relapsed or refractory B-cell non-Hodgkin lymphoma (NHL) (CISL 0602). RIT with ^{131}I-rituximab seemed to be effective in low-grade lymphoma; however, only 1 PR was observed in 11 patients with refractory DLBCL (9% ORR) [35]. Based on this study, a follow-up phase II trial for repeated RIT with ^{131}I-rituximab was conducted (CISL 1013). ^{131}I-rituximab was administered with 4-week interval. In 7 DLBCL patients, 42.9% of ORR (1 in CR and 2 in PR) and 5.0 months of median duration of response were observed [36]. The multicenter, pilot trial of yttrium-90 ibritumomab tiuxetan (Zevalin) consolidation after R-CHOP was performed in a limited stage, bulky DLBCL (CISL 0607). Twenty-one patients with CR or PR after R-CHOP were enrolled, with 3-year PFS and OS of 75.0 and 85.0%, respectively [37].

Furthermore, the CISL has tried alternative regimens for relapsed or refractory DLBCL. ESHAOx [etoposide (E), methylprednisolone (S), high-dose cytarabine (HA), and oxaliplatin (Ox)] for refractory/relapsed aggressive NHL (CISL 0802) and GIDOX [gemcitabine (G), ifosfamide (I), dexamethasone (D), and oxaliplatin (OX)] for B-cell NHL (CISL 0702) were prospectively investigated and resulted in 63 and 52% of ORR, respectively [38, 39]. Both regimens could be considerable options for salvage treatment in relapse or refractory DLBCL.

MZL

As previously mentioned, MZL is relatively common in Koreans and was a primary target for research in the early days of the CISL. We have reported a very wide range of retrospective studies associated with MZL and the sites involved. Nodal, intestinal, and non-gastric MZL were analyzed [40–42], and rare primary sites such as the lungs, thyroid, and Waldeyer's ring were also investigated [43–45]. More recently, we reported that stage I/II MZL was well controlled with a local treatment such as radiation therapy or surgery and showed a good clinical course without additional chemotherapy [46]. However, rituximab has played a significant role in stage IV MZL [47].

In 2006, the CISL conducted phase II trial of rituximab plus CVP (R-CVP) for untreated stage III or IV MZL (CISL 0605). Of the 40 patients, the ORR and median duration of response were 88% and 28.3 months, respectively. The R-CVP can be an effective first-line regimen for advanced stage MZL [48]. Furthermore, we also tried phase II trial for gemcitabine monotherapy in advanced stage MZL; however, the clinical activity was minimal (CISL 0606) [49]. Recently, oxaliplatin and prednisone (Ox-P) combination was investigated in relapsed or refractory MZL (CISL 0905). Salvage Ox-P chemotherapy showed moderate clinical activity (64.7% of ORR) and tolerable toxicity [50].

Other subtypes of B-cell neoplasms

A total of 131 patients with mantle cell lymphoma (MCL) were retrospectively analyzed. The median age was 63 years, and 105 (80.2%) patients had advanced stage of disease. The BM and intestines were involved in 41.2 and 35.1% of patients, respectively. We found simplified MCL international prognostic index (sMIPI) was an important prognostic factor in Korean patients with MCL [51]. In 2012, a phase II study for vorinostat combined with fludarabine, mitoxantrone, and dexamethasone (V-FND) in patients with relapsed or refractory MCL was conducted and resulted in 77.8% ORR and 9.3 months median PFS (CISL 1201). We concluded that V-FND is an effective regimen for relapsed or refractory MCL; however, significant hematologic adverse events including neutropenia (grade 3/4 in 50%) and thrombocytopenia (grade 3/4 in 35%) were not negligible [52].

For Burkitt lymphoma (BL), treatment outcomes of R-hyper-CVAD regimen were retrospectively evaluated in 43 patients, and the 2-year EFS and OS were 70.9 and 81.4%, respectively. However, significant toxicity and unsatisfactory tolerance in Korean patients were observed [53].

In 2016, the CISL retrospectively analyzed 343 patients with FL in Korea. We showed different tendencies compared with those in the Western population, especially with respect to high histologic grade, relatively low stage of disease, and low BCL-2 expression [54].

T-cell neoplasms

ENKTL

For ENKTL, the CISL has introduced the unique performance and outcomes. In 2010, we analyzed 208 patients with ENKTL to evaluate clinical features and outcomes of CNS disease. The Ann Arbor stage, regional lymph node involvement, and NK/T-cell lymphoma prognostic index (NKPI) were used in predicting CNS disease. We concluded that patients with NKPI group I or II do not need a routine CNS evaluation; however, CNS prophylaxis should be considered in patients with NKPI groups II–IV [55]. Next, a multinational retrospective study of ENKTL from the skin or soft tissue was conducted. We analyzed 48 patients with skin/soft tissue primary ENKTL and identified that Korean prognostic index (KPI) score is a useful predictor of prognosis. Moreover, the addition of radiation therapy might have a role in treating localized disease. In metastatic disease, anthracycline-containing regimens were ineffective [56]. Most recently, a prognostic index for NK-cell lymphoma (PINK) after non-anthracycline-based treatment was established by a multinational, retrospective analysis of 527 patients from 38 hospitals in 11 countries. These data showed that age > 60 years, advanced stage, distant lymph node involvement, and non-nasal type were significantly associated with prognosis, and these factors were merged into "PINK." Furthermore, an Epstein–Barr virus (EBV) DNA titer was an independent prognostic factor for the OS. These results were validated in an independent cohort. Thus, PINK and PINK combined with EBV DNA (PINK-E) were established as new prognostic models for risk-adapted treatment approaches [19].

In treating localized ENTKL, three major prospective trials were performed by CISL. Based on the benefits of frontline radiotherapy in the early stages of ENKTL, the first phase II trial of concurrent chemoradiotherapy (CCRT) followed by three cycles of etoposide, ifosfamide, cisplatin, and dexamethasone (VIPD) in stage IE to IIE disease was conducted in 2006 (CISL 0601). Among the 30 patients who completed CCRT, all of them achieved a positive response, with 22 patients in the CR. Twenty-six patients completed the scheduled three cycles of VIPD after CCRT and resulted in 83.3% ORR and 80.0% CR. We concluded that newly diagnosed and early stages of ENKTL are best treated with frontline CCRT [18]. The next trial was CCRT followed by two cycles of VIDL, replacing cisplatin with L-asparaginase due to toxicity (CISL 0803). Among the 30 patients with stages IE and IIE nasal ENKTL, VIDL chemotherapy showed an 87% final CR (26/30), and the estimated 5-year PFS and OS were 73% and 60%, respectively [57]. In 2016, CISL published the results of phase II trial of CCRT with L-asparaginase and methotrexate, ifosfamide, dexamethasone, and L-asparaginase (MIDLE) chemotherapy for stage I/II ENTKL (CISL 1008). We designed a new treatment protocol by adding tri-weekly intravenous or intramuscular L-asparaginase doses during the radiotherapy, and two cycles of MIDLE were repeated every 4 weeks. This protocol showed 82.1% final CR, and the 3-year PFS and OS were 74.1 and 81.5%, respectively. However, concurrent administration of L-asparaginase during CCRT seemed not to be beneficial [58].

PTCL and other subtypes of T-cell neoplasms

For PTCL, the CISL reported a retrospective study on lymphopenia as an independent prognostic indicator to predict the OS and PFS in PTCL-NOS patients treated with anthracycline-containing chemotherapy [59]. Another retrospective study on non-bacterial infections in Asian patients treated with alemtuzumab was conducted and analyzed 182 patients receiving alemtuzumab as frontline, salvage, or part of the conditioning regimen for allogeneic transplantation. Reactivation of cytomegalovirus ($n = 66$), varicella zoster virus ($n = 25$), fungal infections ($n = 31$), and *Pneumocystis jiroveci* pneumonia ($n = 4$) was observed. Thus, we recommended antimicrobial prophylaxis in Asian patients receiving alemtuzumab [60].

The CISL has focused on the innovative prospective trials on T-cell neoplasms. We designed a prospective phase II study of alemtuzumab and DHAP (A-DHAP) for relapsed PTCL or ENKTL and briefly reported 50.0% ORR in 16 patients (CISL 0604) [61]. Moreover, the CISL conducted a phase I study of bortezomib plus CHOP (Vel-CHOP) regimen in patients with advanced, aggressive T- or NK/T-cell lymphoma in 2007 (CISL 0701). Thirteen patients with stage III/IV aggressive T-cell lymphoma were treated with Vel-CHOP as a first-line therapy, and 61.5% CR was reported. We concluded that Vel-CHOP could be a safe regimen and recommended a bortezomib dose of 1.6 mg/m^2 for subsequent phase II trial [62]. Based on this study, we consequently performed phase II trial of Vel-CHOP for a first-line treatment in advanced T-cell lymphoma (CISL 0705). Forty-six patients with various subtypes of T-cell lymphoma were enrolled, and 30 (65.2%) patients achieved CR. Consequently, 3-year PFS and OS were 35 and 47%, respectively [63]. Another phase I study of everolimus and CHOP was performed in newly diagnosed PTCL patients, and everolimus plus CHOP regimen could be feasible and effective (CISL 1108) [64]. Sequentially, a phase II study was conducted on 30 patients with PTCL. The ORR was 90% with CR in 17 patients and PR in 10 patients. Interestingly, the efficacy was associated with loss of PTEN [65]. We investigated the salvage chemotherapy using gemcitabine, dexamethasone, and cisplatin (GDP) for patients with relapsed or refractory PTCL (CISL 1003). Fourteen patients with PTCL-NOS and 4 patients with AITL were enrolled, and 12 had a CR and 6 had a PR. The median PFS was 9.3 months. GDP is a highly effective treatment regimen for relapsed or refractory PTCLs and could be an optional salvage treatment [66].

Ongoing clinical trials and future perspectives

Since 2006, Korean researchers for lymphoid neoplasms and the CISL have focused on lymphoma subtypes relatively common in Korea, such as DLBCL, MZL, ENKTL, and PTCL. Moreover, clinical studies have been conducted in collaboration with specialists, such as pathologists, radiologists, radiotherapists, and physicians of diagnostic laboratories and nuclear medicine. As of November 2017, there were 13 ongoing studies in the CISL, with 6 phase II or III trials in B-cell neoplasms, 3 phase II trials in T-cell neoplasms, and 4 prospective cohort or registry studies. Furthermore, several prospective cohort studies and clinical trials on DLBCL, MCL, and primary CNS lymphoma have also been planned. In the future, we plan to continue working with researchers from various countries in Asia to improve the survival of lymphoma patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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