Treatment patterns and clinical outcomes in patients with lymphoma aged ≥90 years: A single-center retrospective study

NOBUHITO HARA[1,2], NOZOMI OKAHASHI[2], EI HOSHINO[2], MASAYUKI KUBO[3] and MASAYUKI TAKEDA[1]

[1]Department of Cancer Genomics and Medical Oncology, Nara Medical University, Kashihara, Nara 634-8521, Japan; [2]Department of Hematology, Saiseikai Chuwa Hospital, Sakurai, Nara 633-0054, Japan; [3]Department of Hematology, Nara Medical University, Kashihara, Nara 634-8521, Japan

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Abstract. The optimal treatment strategy for malignant lymphoma in patients aged ≥90 years remains unclear. This single-center retrospective study evaluated treatment patterns and outcomes in 14 patients aged ≥90 years diagnosed with lymphoma between January 2020 and April 2026. Clinical characteristics, treatments, adverse events, and overall survival (OS) were retrospectively analyzed. The median age was 92 years (range, 90-95 years), and diffuse large B-cell lymphoma was the most common subtype (57%). Initial treatments included chemotherapy (n=10), steroid monotherapy (n=3), and watchful waiting (n=1). All patients receiving combination chemotherapy required dose reductions to ≤70% of standard intensity. The curative-intent chemotherapy group (n=8) had a median OS of 374 days, compared with 46 days in the palliative-intent group (n=4; log-rank P=0.00299). Grade ≥3 adverse events occurred in 90% of chemotherapy-treated patients, with 50% developing infections. Curative-intent chemotherapy was associated with longer survival in selected patients aged ≥90 years, although treatment-selection bias precludes causal inference. Substantial toxicity persisted despite dose reductions, emphasizing the importance of individualized treatment decisions based on functional status, comorbidities, and patient preferences.

Correspondence to: Professor Masayuki Takeda, Department of Cancer Genomics and Medical Oncology, Nara Medical University, 840 Shijo-Cho, Kashihara, Nara 634-8521, Japan
E-mail: takeda-m@naramed-u.ac.jp

Abbreviations: ADL, activities of daily living; AITL, angioimmunoblastic T-cell lymphoma; BSC, best supportive care; CCI, Charlson comorbidity index; CR, complete response; CRP, C-reactive protein; CTCAE, Common Terminology Criteria for Adverse Events; DLBCL, diffuse large B-cell lymphoma; ECOG-PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; IPI, International Prognostic Index; LDH, lactate dehydrogenase; OS, overall survival; PD, progressive disease; PR, partial response; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisone; SD, stable disease; sIL-2R, soluble interleukin-2 receptor

Key words: malignant lymphoma, super-elderly, patients aged ≥90 years, real-world data, frailty, chemotherapy, survival outcomes, retrospective study

Introduction

The burden of lymphoma among older adults has continued to increase and is expected to further increase with population aging. In line with this, malignant lymphoma has become one of the major hematologic malignancies (1). Non-Hodgkin lymphoma, in particular, has been found to primarily affect older individuals. Although recent advances in treatment have improved patient outcomes, the optimal treatment strategy for super-elderly patients, particularly those aged ≥90 years, has yet to be established. Considering the older patients are often underrepresented in clinical trials, available evidence has been largely derived from relatively younger or fitter patients (2). Although several prospective and retrospective studies have evaluated chemotherapy in patients with malignant lymphoma aged ≥80 years (3,4), evidence specifically focusing on patients aged ≥90 years remains extremely limited. In real-world clinical practice, individualized treatment approaches that account for frailty, comorbidities, organ function, and disease characteristics are required. Unfortunately, decisions regarding the indication for chemotherapy and treatment intensity are often individualized based on physician judgment.

To facilitate the accumulation of evidence for the management of the growing population of super-elderly patients with lymphoma, this single-center retrospective investigated real-world treatment patterns among patients with lymphoma aged ≥90 years.

Materials and methods

Study design and participants. This single-center retrospective observational study included patients with malignant lymphoma who received medical care at Saiseikai Chuwa Hospital between January 1, 2020 and April 1, 2026. Patients were eligible for inclusion if they met all of the following criteria: (1) age ≥90 years at the time of diagnosis; (2) a

pathologically confirmed diagnosis of malignant lymphoma; (3) diagnosis or determination of the treatment strategy at our institution between January 1, 2020 and April 1, 2026; and (4) availability of relevant clinical information, including patient characteristics, treatment details, and outcomes, from the medical records.

Patients were excluded if they met any of the following criteria: (1) they were considered unsuitable for inclusion by the principal investigator; (2) they had a concurrent malignancy other than malignant lymphoma; (3) key outcome data, including survival information, could not be obtained from the medical records; or (4) they received minimal clinical management at our institution and adequate follow-up information was unavailable. After applying these eligibility criteria, 14 patients were included in the study.

Clinical data were collected retrospectively from electronic medical records. The electronic medical records were accessed and data were retrieved for analysis between April 23, 2026 and August 18, 2026. Given that this retrospective study used existing data, the requirement for informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Saiseikai Chuwa Hospital (approval number: 08-002).

Data collection. The following baseline characteristics were extracted: age at initial visit, sex, height, and body weight. Disease-related variables included the date of pathological diagnosis (i.e., the date of specimen submission for pathological evaluation), histological subtype, Ann Arbor stage, presence of B symptoms (fever, weight loss, and night sweats), and central nervous system (CNS) involvement. Additionally, the presence and sites of extranodal disease and bulky lesions (maximum diameter ≥10 cm) were recorded. Laboratory data at diagnosis included lactate dehydrogenase (LDH), soluble interleukin-2 receptor (sIL-2R), hemoglobin, serum albumin, creatinine, estimated glomerular filtration rate (eGFR), and C-reactive protein (CRP). LDH levels were classified as normal or elevated based on institutional reference values. For patients with aggressive lymphoma or those clinically suspected to have aggressive disease, the International Prognostic Index (IPI) was assessed.

Geriatric assessment. Performance status was evaluated using the Eastern Cooperative Oncology Group performance status (ECOG) Performance Status scale. Activities of daily living (ADL) were categorized into three levels: independent, partially dependent, and fully dependent. If these variables were not explicitly documented, they were retrospectively estimated based on detailed clinical documentation when sufficient information was available or confirmed with the attending physician. Comorbidities were assessed using the Charlson Comorbidity Index (CCI), and the number of medications at initial presentation was recorded. The presence of dementia was determined based on medical records.

Treatment and outcomes. Initial treatment was categorized as follows: steroid monotherapy, single-agent chemotherapy, combination chemotherapy, radiotherapy alone, chemoradiotherapy, or best supportive care (BSC). Specific chemotherapy regimens were also recorded. For patients receiving chemotherapy, the number of patients requiring dose reduction to ≤70% intensity and the number of treatment cycles were collected. Treatment start and end dates, as well as treatment discontinuation and its reasons, were recorded. Treatment discontinuation was defined as failure to complete the planned initial course of therapy, excluding completion of maintenance therapy. Information on second-line and subsequent treatments, including salvage therapy, was also collected.

Adverse events during treatment were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Grade ≥3 leukopenia, neutropenia, febrile neutropenia, infections, and all grade ≥3 adverse events were recorded. Hospitalizations during treatment (excluding the planned admissions for chemotherapy initiation) were also documented. Available PET/CT and/or CT findings were used to classify treatment response as complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) according to the Lugano classification (5). Best response, date of response evaluation, relapse status, and date of relapse were recorded.

Survival analysis. Overall survival (OS) was defined as the duration from the date of pathological diagnosis to death or last follow-up. Data on survival status, date of death, cause of death (lymphoma-related, treatment-related, or others), and last confirmed survival date were collected. Survival curves were estimated using the Kaplan-Meier method, and differences between groups were evaluated using the log-rank test. Prognostic differences among treatment groups were also analyzed. Owing to the small sample size, multivariate analysis was not performed. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (6), with a P-value of <0.05 indicating statistical significance.

Definition of missing data. Missing data were defined as data that should have been collected but were unavailable. Data labeled as 'not applicable (NA)' referred to variables that were not relevant to a given patient.

Results

A total of 14 patients aged ≥90 years (median age, 92 years; range, 90-95 years) were included in this study, among whom 6 (43%) were male and 8 (57%) were female.

Baseline characteristics (Table I). The most common histological subtype was diffuse large B-cell lymphoma (DLBCL) (n=8, 57%), followed by unclassified B-cell lymphoma (n=3, 21%), marginal zone lymphoma (n=1, 7%), angioimmunoblastic T-cell lymphoma (AITL) (n=1, 7%), and unclassified T-cell lymphoma (n=1, 7%). Based on clinical classification, 9 (64%), 2 (14%), and 3 patients (21%) had aggressive, indolent, and unclassified lymphoma, respectively. According to Ann Arbor staging, 5 (36%) and 9 patients (64%) had stage I-II and stage III-IV disease, respectively.

B symptoms were present in 4 patients (29%). Extranodal involvement was observed in 12 patients (86%), and bulky disease (≥10 cm) was present in 4 patients (29%).

Table I. Baseline characteristics of patients aged ≥90 years with malignant lymphoma (n=14).

Variable	Total (n=14)
Age, years	
Median (range)	92 (90-95)
Sex	
Male, n (%)	6 (43)
Female, n (%)	8 (57)
Histological subtype	
Diffuse large B-cell lymphoma, n (%)	8 (57)
Marginal zone cell lymphoma, n (%)	1 (7)
B-cell lymphoma (unclassified), n (%)	3 (21)
AITL, n (%)	1 (7)
T-cell lymphoma (unclassified), n (%)	1 (7)
Disease classification	
Aggressive lymphoma, n (%)	9 (64)
Indolent lymphoma, n (%)	2 (14)
Unclassified, n (%)	3 (21)
Ann Arbor stage	
I-II, n (%)	5 (36)
III-IV, n (%)	9 (64)
B symptoms	
Present, n (%)	4 (29)
Extranodal involvement	
Present, n (%)	12 (86)
Bulky disease (≥10 cm)	
Present, n (%)	4 (29)
Laboratory data at diagnosis	
Lactate dehydrogenase elevated, n (%)	10 (71)
sIL-2R, U/ml, and median (range)	2065 (207-50464)
Hemoglobin, g/dl, median (range)	10.7 (3.8-15.4)
Albumin, g/dl, median (range)	3.7 (1.1-4.3)
Creatinine, mg/dl, median (range)	0.92 (0.49-4.63)
eGFR, ml/min/1.73 m^2, median (range)	51.05 (7.3-85.7)
CRP, mg/dl, and median (range)	1.183 (0.04-14.22)
IPI (aggressive lymphoma, n=9)	
Low/Low-intermediate ≤2, n (%)	4 (44)
High-intermediate/High ≥3, n (%)	5 (56)
ECOG performance status	
0-1, n (%)	8 (57)
≥2, n (%)	6 (43)
Activities of daily living	
Independent, n (%)	7 (50)
Partially dependent, n (%)	7 (50)
Fully dependent, n (%)	0 (0)
Charlson Comorbidity Index	
Median (range)	7 (6–8)
Dementia	
Present, n (%)	1 (7)
Number of medications	
Median (range)	5 (0-12)

Demographic, clinical, laboratory, and geriatric assessment data at diagnosis are summarized. AITL, angioimmunoblastic T-cell lymphoma; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; IPI, International Prognostic Index; ECOG, Eastern Cooperative Oncology Group.

Upon diagnosis, elevated LDH was observed in 10 patients (71%). Median sIL-2R level was 2065 U/ml (range, 207-50,464 U/ml). Median hemoglobin, albumin, creatinine, eGFR, and CRP were 10.7 g/dl (range, 3.8-15.4 g/dl), 3.7 g/dl (range, 1.1-4.3), 0.92 mg/dl (range, 0.49-4.63 mg/dl), 51.05 ml/min/1.73 m^2 (range, 7.3-85.7 ml/min/1.73 m^2), and 1.183 mg/dl (range, 0.04-14.22 mg/dl), respectively.

Among the 9 patients with aggressive lymphoma, 4 (44%) and 5 (56%) had an IPI of low or low-intermediate (≤2) and high-intermediate or high (≥3), respectively.

ECOG Performance Status was 0-1 and ≥2 in 8 (57%) and 6 patients (43%), respectively. Regarding ADL, 7 patients (50%) were independent, whereas 7 (50%) were partially dependent, with no patient being fully dependent. The median CCI was 7 (range, 6-8). Dementia was present in 1 patient (7%), and the median number of medications was 5 (range, 0-12). There were no missing data for the variables presented in Table I, including IPI scores, ADL assessments, and laboratory values. Height and weight data were unavailable for some patients; however, these data were complete for all patients who received combination chemotherapy, for whom body surface area was calculated to determine chemotherapy dosing. Radiological assessment of CNS involvement at our institution was unavailable for some patients; however, none had symptoms suggestive of CNS involvement at initial presentation.

Initial treatment according to histological classification (Table II). The initial treatment comprised chemotherapy, steroid monotherapy, and watchful waiting in 10 (71%), 3 (21%), and 1 patient (7%), respectively.

Among the 9 patients with aggressive lymphoma, 8 (89%) received chemotherapy, 1 (11%) received steroid monotherapy, and none underwent watchful waiting. In contrast, among the 2 patients with indolent lymphoma, 1 (50%) received chemotherapy, while the other (50%) received watchful waiting. Among the 3 patients in the unclassified group, 1 (33%) received chemotherapy, while 2 (67%) received steroid monotherapy.

Among the 10 patients who received chemotherapy, 8 (80%) received combination chemotherapy, while 2 (20%) received single-agent chemotherapy. Combination chemotherapy was administered to 7 of the 8 patients with aggressive cases and 1 of 1 unclassified patient, whereas no indolent cases received combination therapy. The regimen details among the 8 patients who received combination chemotherapy were as follows: 4 received R-CVP, 2 received CVP alone, 1 was initially treated with R-CVP but subsequently switched to prednisone, rituximab, cyclophosphamide, doxorubicin, and polatuzumab vedotin (PR-CHP) due to treatment modification, and 1 was initially treated with R-CVP but subsequently switched to R-CHP.

Treatment details of patients receiving combination chemotherapy (Table III). All patients receiving combination chemotherapy (n=8, 100%) required dose reduction of the cytotoxic agents to ≤70% of their standard dose intensity. Implementation of dose reduction started from the first cycle in 7 patients but from the second cycle in 1 patient due to treatment-related adverse events. The dose of rituximab, whether administered in combination or as monotherapy, was

Table II. Treatment characteristics of patients with malignant lymphoma aged ≥90 years stratified according to histological classification (n=14).

Initial treatment	Total (n=14)	Aggressive (n=9)	Indolent (n=2)	Unclassified (n=3)
Chemotherapy, n (%)	10 (71)	8 (89)	1 (50)	1 (33)
Combination chemotherapy	8	7	0	1
Single-agent chemotherapy	2	1	1	0
Steroid monotherapy, n (%)	3 (21)	1 (11)	0 (0)	2 (67)
Watchful waiting, n (%)	1(7)	0 (0)	1 (50)	0 (0)

Initial treatment strategies are summarized for all patients and according to lymphoma subtype (aggressive, indolent, and unclassified).

Table III. Treatment details of patients receiving combination chemotherapy (n=8), stratified according to histological subtype.

Combination chemotherapy	Total (n=8)	Aggressive (n=7)	Indolent (n=0)	Unclassified (n=1)
Dose reduction to ≤70%, n/N (%)	8(100)	7 (100)	NA	1 (100)
No. of cycles, median (range)	4.5(1-6)	6 (1-6)	NA	1 (NP)
Treatment discontinuation, n/N (%)	4 (50)	3 (43)	NA	1 (100)
Second-line therapy, n (%)	4 (50)	4 (57)	NA	0 (0)

Dose reduction, number of treatment cycles, treatment discontinuation, and use of second-line therapy are summarized for the overall cohort and lymphoma subtype.

not reduced by more than 30% in any patient. The median number of cycles was 4.5 (range, 1-6), with a median of 6 cycles (range, 1-6) being administered among patients with aggressive lymphoma. Treatment discontinuation occurred in 4 patients (50%), including 3 of the 7 patients with aggressive lymphoma (43%) and 1 of 1 unclassified patient (100%). Second-line therapy was administered to 4 patients (50%), all of whom had aggressive lymphoma. The reasons for treatment discontinuation were Mycoplasma pneumonia in one patient with diffuse large B-cell lymphoma (DLBCL), worsening lymphoma-related symptoms in one patient with AITL, gastrointestinal bleeding in one patient with unclassified lymphoma, and deterioration in performance status in one patient with DLBCL. These patients discontinued combination chemotherapy after completing 3, 1, 1, and 2 cycles, respectively.

Treatment outcomes and comparison between the curative and palliative-intent groups (excluding indolent lymphoma). Treatment strategies for the patients, excluding those with indolent lymphoma, were stratified into curative chemotherapy (multiagent chemotherapy, n=8) and palliative intent (steroid monotherapy, single-agent chemotherapy, or watchful waiting, n=4).

Of the patients with unclassified lymphoma, one patient with T-cell lymphoma was considered to have indolent disease based on pathological findings and was therefore included in the indolent lymphoma group and excluded from this analysis. Conversely, the three patients with unclassified B-cell lymphoma had clinical features strongly suggestive of aggressive disease, although a definitive pathological classification could not be established. These patients were therefore assigned to the curative- or palliative-intent group according to the treatment strategy while retaining their designation as having unclassified lymphoma.

Baseline characteristics between treatment groups (Table IV). Comparison of baseline characteristics demonstrated a clear difference in patient condition between the two groups. Poor performance status (ECOG ≥2) was more frequently observed in the palliative group than in the curative group. Similarly, elevated tumor burden and adverse biological markers, including high soluble IL-2 receptor levels (≥2,000 U/ml), elevated LDH, and presence of B symptoms, were more prevalent in the palliative group than in the curative group. Advanced-stage disease (Ann Arbor stage III-IV) was also more common in the palliative-intent group than in the curative group.

Moreover, the comorbidity burden was higher in the palliative group than in the curative group, with a CCI of ≥7 observed more frequently in the former. Taken together, patients selected for curative-intent multiagent chemotherapy generally had more favorable baseline functional status and disease-related risk profiles, whereas those in the palliative group tended to have poorer performance status and higher systemic disease burden.

Treatment response and survival outcomes (Table V). The curative chemotherapy group (n=8) had an overall response rate of 50%, including CR in 2 patients (25%) and PR in 2 patients (25%). SD and PD were observed in 1 patient each (12.5% each), whereas 2 patients (25%) did not undergo

Table IV. Baseline characteristics of patients with malignant lymphoma aged ≥90 years stratified according to treatment strategy (curative-intent vs. palliative-intent groups).

Group	ECOG-PS ≥2 (%)	sIL2R ≥2,000 (%)	High LDH (≥ULN) (%)	B symptoms present (%)	High CCI (≥7) (%)	Stage 3,4
Curative Chemotherapy (2+ agents) Group (n=8)	2 (25)	4 (50)	6 (75)	2 (25)	5 (63)	3 (38)
Steroid Monotherapy + Chemotherapy (1 agent) + Watchful waiting Group (n=4)	4 (100)	3 (75)	3 (75)	2 (50)	3 (75)	4 (100)

Performance status, laboratory findings, disease burden and comorbidity indices are compared between treatment groups. sIL-2R, soluble interleukin-2 receptor; LDH, lactate dehydrogenase; CCI, Charlson comorbidity index; ULN, upper limit of normal.

Table V. Treatment response and survival outcomes among patients with malignant lymphoma aged ≥90 years stratified according to treatment strategy.

Treatment group	CR, n (%)	PR, n (%)	SD, n (%)	PD, n (%)	Not evaluated, n (%)	Median survival, days (range)	90-day survival, (%)
Curative Chemotherapy (2+ agents) Group (n=8)	2 (25)	2 (25)	1 (12.5)	1 (12.5)	2 (25)	374 (20-1991)	88
Steroid Monotherapy + Chemotherapy (1 agent) + Watchful waiting group (n=4)	0 (0)	0 (0)	0 (0)	0 (0)	4 (100)	46 (2-139)	25

CR, complete response; OS, median overall survival; PD, progressive disease; PR, partial response; SD, stable disease.

response evaluation. The median OS was 374 days (range, 20-1991), whereas the 90-day OS rate was 87.5%.

In contrast, the palliative-intent group showed no objective responses. No patients achieved CR, PR, SD, or PD assessment outcomes given that treatment effects could not be evaluated in 4 patients (100%). The median survival was 46 days (range, 2-139), whereas the 90-day OS rate was 25.0%.

Survival outcomes according to treatment strategy. A comparison of survival outcomes between the palliative and curative-intent treatment groups is presented in Fig. 1. At 90 days, the survival rate was 25.0% [95% confidence interval (CI), 0.9-66.5] and 87.5% (95% CI, 38.7-98.1) in the palliative (n=4) and curative chemotherapy groups (n=8), respectively. The median OS was significantly shorter in the palliative group (46 days; 95% CI, 2-not available) than in the curative group (374 days; 95% CI, 20-not available; log-rank test, P=0.00299). These results demonstrated that patients who did not receive curative-intent chemotherapy exhibited significantly inferior survival outcomes than did those who received multiagent chemotherapy.

Adverse events in patients receiving chemotherapy (Table VI). Adverse events among patients who received chemotherapy (including combination chemotherapy, single-agent etoposide, or rituximab monotherapy) were evaluated according to CTCAE version 5.0. Those who received steroid monotherapy or BSC were excluded from this analysis. Grade ≥3 hematological toxicities were frequently observed. Leukopenia and neutropenia occurred in 5 patients (50%) each. Febrile neutropenia was observed in 4 patients (40%), whereas grade ≥3 anemia was observed in 4 patients (40%). None of the patients developed thrombocytopenia (0%).

Grade ≥3 infections occurred in 5 patients (50%). Infectious complications included cytomegalovirus retinitis, lymphadenitis/cellulitis/streptococcal bacteremia, Mycoplasma pneumonia, oral candidiasis/urinary tract infection, and bacteremia/urinary tract infection. Other grade ≥3 adverse events, including depression, hyponatremia, eosinophilia with eosinophilic encephalopathy, and upper gastrointestinal bleeding, were observed in 4 patients (40%). Overall, any grade ≥3 adverse event occurred in 9 patients (90%), with 9 patients (90%) requiring hospitalization during treatment. All nine patients were hospitalized during induction therapy. Furthermore, three patients required readmission or prolonged hospitalization due to lymphoma progression, three were hospitalized due to treatment-related adverse events, and two required readmission for supportive care during subsequent chemotherapy cycles.

Discussion

The current study provides clinically relevant real-world data focusing on super-elderly patients with lymphoma aged

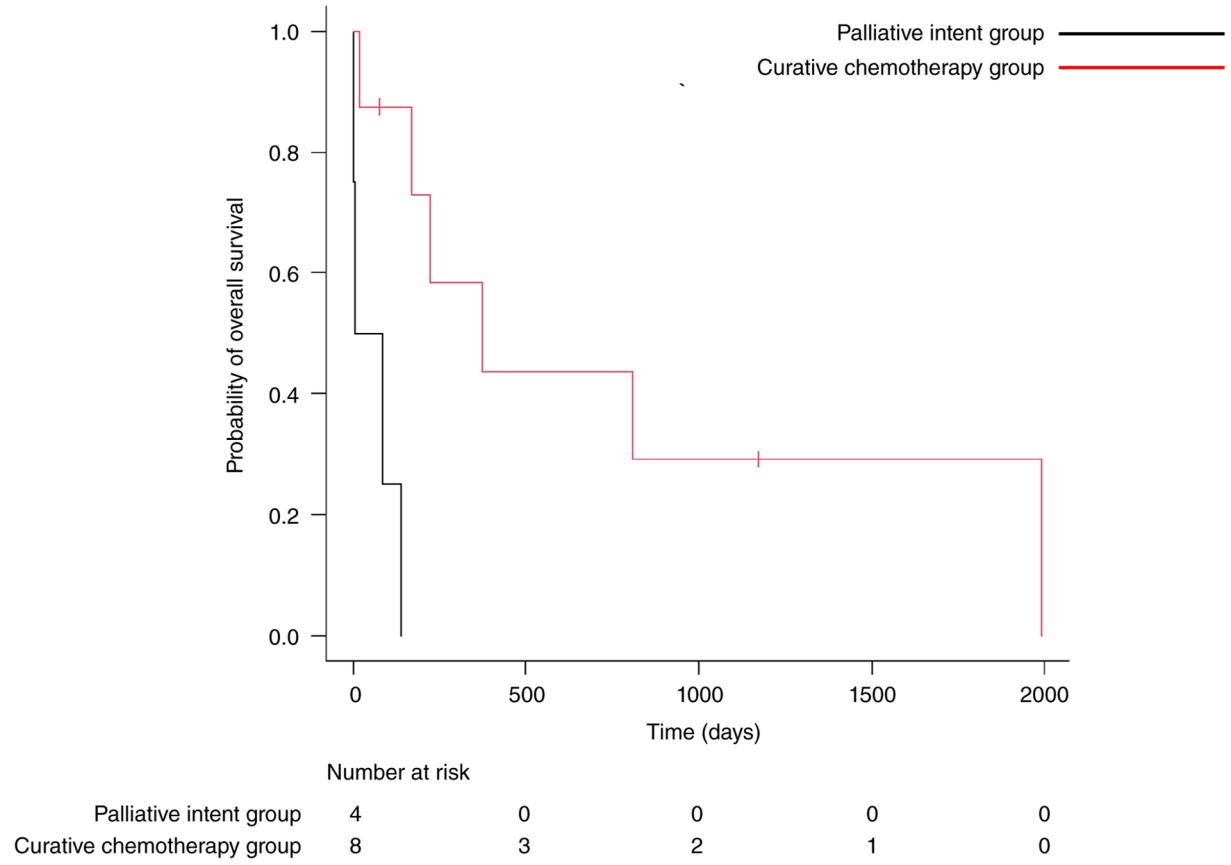


Figure 1. Overall survival in patients with malignant lymphoma aged ≥90 years stratified according to treatment strategy. Kaplan-Meier survival curves comparing the palliative-intent group (black line) and the curative-intent combination chemotherapy group (red line) are shown. The number of patients at risk at each time point is displayed below the graph.

≥90 years. This age group has been largely excluded from clinical trials, with large cohort data remaining scarce even in retrospective analyses. Although a previous large retrospective study by Trebouet *et al* (7) included elderly patients with lymphoma, the cohort primarily comprised cases diagnosed between 1990 and 2012 and therefore included a substantial proportion of patients who did not receive rituximab-based therapy. Consequently, evidence regarding treatment selection and outcomes in the era of currently available agents remains considerably limited. In this context, our findings provide valuable insights into the real-world treatment patterns and outcomes of very elderly patients with lymphoma.

In this particular cohort, treatment decisions are influenced not only by tumor-related factors (e.g., tumor burden, elevated LDH, sIL-2R, and advanced stage) but also, and more importantly, by the patient's overall condition (e.g., Eastern Cooperative Oncology ECOG-PS and CCI). Notably, all patients in the palliative care group had stage III or higher disease and an ECOG-PS of ≥2, suggesting that these parameters played a decisive role in treatment selection. These findings indicate that therapeutic decision-making in this cohort was primarily driven not only by tumor aggressiveness but also by; treatment tolerance', reflecting physiological reserve and overall functional status.

Regarding treatment efficacy, the curative-intent combination chemotherapy group achieved an overall response rate of 50% (CR, 25%; PR, 25%) with a median OS of 374 days. Despite the difficulty of direct comparisons, Trebouet *et al* (7) reported a median OS of 8.12 months in treated patients with aggressive non-Hodgkin lymphoma. In comparison, our cohort demonstrated a more favorable OS. These findings suggest that carefully selected individuals may derive meaningful benefit from chemotherapy and may also reflect improvements in modern therapeutic strategies for elderly patients, even among those patients aged ≥90 years. Importantly, these results support the notion that chronological age alone should not be the sole criterion for excluding patients with aggressive lymphomas, such as DLBCL, from active treatment.

In contrast, the palliative care group demonstrated extremely poor outcomes, with a median survival of 46 days and a 90-day survival rate of 25%. This poor prognosis could likely be attributed to advanced disease burden, poor performance status, and a high CCI, all of which strongly contributed to early mortality. Importantly, the observed survival differences between the treatment groups should be considered descriptive and hypothesis-generating rather than evidence of a treatment effect, given the extremely small sample size and substantial treatment-selection bias. In particular, the small number of patients in the palliative care group precludes robust statistical inference. Moreover, patients selected for curative-intent treatment generally had better baseline functional status and physiological reserve than those receiving palliative care. Therefore, the apparent separation of the survival curves may largely reflect differences in baseline patient characteristics,

Table VI. Grade ≥3 adverse events and hospitalization rates in patients aged ≥90 years receiving chemotherapy for malignant lymphoma.

Adverse events	Grade ≥3, n (%)
Leukopenia	5 (50)
Neutropenia	5 (50)
Febrile neutropenia	4 (40)
Infection	5 (50)
Anemia	4 (40)
Thrombocytopenia	0 (0)
Other grade ≥3 adverse events	4 (40)
Any grade ≥3 adverse event	9 (90)
Hospitalization during treatment	9 (90)

and a causal effect of treatment on survival cannot be inferred from this comparison. Frailty is increasingly recognized as a key consideration in treatment decision-making for older patients with lymphoma. Several studies have suggested that frailty assessment may better capture physiological vulnerability than tumor-related factors alone, highlighting its important role in therapeutic decision-making (8,9). The treatment regimens used in the present cohort also warrant careful consideration. Of the two patients who received CVP without rituximab, one had AITL, for which rituximab was not indicated. The other patient had B-cell lymphoma and initially received CVP; however, the disease progressed rapidly, and the patient died before rituximab could be administered. Thus, rituximab was incorporated into the treatment of patients with B-cell lymphoma when its administration was considered clinically feasible. Anthracycline-free regimens, such as R-CVP, were frequently selected because of concerns regarding the tolerability of doxorubicin in this exceptionally old population, based on each patient's overall condition, comorbidities, organ function, and functional status. Therefore, the frequent use of R-CVP in this cohort reflected individualized assessments of treatment tolerability rather than a general strategy of avoiding anthracycline-containing therapy.

Regarding safety, 90% of patients receiving chemotherapy developed grade ≥3 adverse events. In particular, 50% of patients developed infections, while 90% required hospitalization, highlighting the substantial treatment-related toxicity in this population. These findings indicate that even with dose-reduced chemotherapy (≤70% of standard intensity), safety remains a major concern in patients aged ≥90 years. Moreover, the high frequency of severe toxicity despite dose reduction suggests that a simple dose-reduction strategy does not necessarily ensure safety in this super-elderly population. Our findings therefore emphasize the importance of intensive supportive care.

R-miniCHOP is an important treatment option for selected patients aged >80 years with DLBCL (10). However, patients aged ≥90 years remain underrepresented in the available evidence, and the optimal treatment strategy for this population remains uncertain. Notably, substantial toxicity was observed in the present cohort despite dose attenuation and the frequent omission of anthracyclines in patients considered unlikely to tolerate them. These findings suggest that reducing treatment intensity alone may not ensure tolerability in patients aged ≥90 years and highlight the importance of individualized treatment selection.

Finally, this study has several limitations, including its single-center retrospective design, extremely small sample size (n=14), substantial treatment-selection bias, lack of multivariable analysis, and heterogeneity in follow-up and assessment methods. Importantly, the study was not statistically powered to detect differences in survival between the treatment groups, particularly given that the palliative care group included only four patients. Therefore, the survival analysis should be considered exploratory and descriptive, and the observed separation of the survival curves should not be interpreted as evidence of the efficacy of curative-intent treatment. Patients who received curative-intent treatment were generally in better baseline condition, whereas those receiving palliative care exhibited advanced frailty and organ dysfunction. Accordingly, direct comparisons between groups should be interpreted with caution.

Furthermore, diagnostic selection bias represents a major limitation of the present study. Among patients aged ≥90 years who presented to our institution, those with poor general condition, in whom sufficient diagnostic evaluation could not be performed and who were instead managed with BSC or end-of-life care despite suspected malignant lymphoma, were not included in our analysis. Because of the retrospective nature of this study, the number of patients who were excluded because they were unable to undergo biopsy could not be reliably determined. Patients who did not undergo biopsy were not necessarily recorded as having lymphoma in the electronic medical records and therefore could not be systematically identified retrospectively. Furthermore, some extremely frail patients with suspected lymphoma may not have been referred to our institution from surrounding hospitals or clinics because invasive diagnostic procedures, including biopsy, were considered infeasible. Consequently, the present cohort may not fully represent the spectrum of patients aged ≥90 years with suspected lymphoma encountered in real-world clinical practice. Our findings should therefore be interpreted as reflecting the outcomes of patients aged ≥90 years with pathologically confirmed lymphoma rather than those of the broader population of patients with suspected lymphoma in this age group. The natural history, prognosis, and treatment needs of patients who are unable to complete diagnostic evaluation because of severe frailty or rapid clinical deterioration warrant further investigation. Collectively, these limitations restrict the generalizability of our findings, and larger, multicenter prospective studies are needed to validate our observations.

Despite these limitations, the present study provides descriptive real-world evidence that active chemotherapy was feasible in a subset of carefully selected patients aged ≥90 years, although treatment-related toxicity remained substantial. Given the substantial potential for treatment-selection bias, the observed survival outcomes should not be interpreted as evidence of a survival benefit from chemotherapy in this population. Rather, our findings indicate that chronological age alone may be insufficient to guide treatment decisions and that treatment selection should consider functional status, comorbidities, physiological reserve, patient preferences, and anticipated treatment toxicity. Larger, multicenter studies are

needed to identify patients aged ≥90 years who may benefit from active treatment and to determine optimal treatment strategies for this population.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

NH conceptualized the manuscript. NH, NO, EH MK, and MT acquired and interpretated the data. NH and MT confirm the authenticity of all the raw data. NH wrote the original draft, and NH and MT wrote, reviewed and edited the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

This retrospective study was conducted using anonymized clinical data extracted from existing medical records. The requirement for informed consent was waived due to the retrospective nature of the study. The study was performed following the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Saiseikai Chuwa Hospital (approval no. 08-002).

Patient consent for publication

Not applicable.

Competing interests

Dr. Takeda received honoraria from Chugai Pharmaceutical, AstraZeneca K.K., Bristol-Myers Squibb Company, Novartis Pharma K.K., and Ono Pharmaceutical. The other authors declare that they have no competing interests.

Use of artificial intelligence

During the preparation of this work, artificial intelligence tools were used to improve the readability and language of the manuscript and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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