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REVIEW ARTICLE

# Guidelines for the management of cutaneous lymphomas (2011): A consensus statement by the Japanese Skin Cancer Society – Lymphoma Study Group

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## ABSTRACT

**In 2010, the first Japanese edition of guidelines for the management of cutaneous lymphoma was published jointly by the Japanese Dermatological Association (JDA) and the Japanese Skin Cancer Society (JSCS) – Lymphoma Study Group. Because the guidelines were revised in 2011 based on the most recent data, we summarized the revised guidelines in English for two reasons: (i) to inform overseas clinicians about our way of managing common types of cutaneous lymphomas such as mycosis fungoides/Sézary syndrome; and (ii) to introduce Japanese guidelines for lymphomas peculiar to Asia, such as adult T-cell leukemia/lymphoma and extranodal natural killer/T-cell lymphoma, nasal type. References that provide scientific evidence for these guidelines have been selected by the JSCS – Lymphoma Study Group. These guidelines, together with the degrees of recommendation, have been made in the context of limited medical treatment resources, and standard medical practice within the framework of the Japanese National Health Insurance system.**

**Key words: adult T-cell leukemia/lymphoma, cutaneous lymphoma, guideline, mycosis fungoides, Sézary syndrome.**

## INTRODUCTION

A number of guidelines on the management of cutaneous lymphoma have already been published in Europe and North America. However, the prevalence and clinical types of cutaneous lymphoma vary among different ethnic groups, and medical systems vary from country to country. As a result, the unmodified European/US guidelines may not be well-suited for use in Japan. We wanted to provide a "best treatment" consensus on clinical practice guidelines for cutaneous lymphoma, based on the actual situation in Japan.

In these guidelines, the diagnosis of cutaneous lymphoma is based on classifications from the World Health Organization (WHO) and European Organization for Research and Treatment of Cancer, Cutaneous Lymphomas Task Force (EORTC),[1] and on the 4th edition of the WHO classification published in 2008.[2] The staging and classification of mycosis fungoides (MF)/Sézary syndrome (SS) are based on the tumor

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–node–metastasis (TNM) staging from the International Society for Cutaneous Lymphomas (ISCL) group.[3] For cutaneous lymphomas other than MF/SS, we decided to use the TNM staging system proposed by the ISCL[4] rather than the conventional Ann Arbor classification system.

The British group,[5] EORTC[6] and European Society for Medical Oncology (ESMO)[7] each issued treatment guidelines for MF/SS. In 2009, using published work and overseas guidelines for references, we published the first edition of guidelines based on the actual situation of cutaneous lymphoma in Japan.[8] Because the guidelines were revised in 2011 based on the most recent data, we summarized the revised guidelines in English for two reasons: (i) to inform overseas clinicians about our way of managing common types of cutaneous lymphomas such as MF/SS; and (ii) to introduce Japanese guidelines for lymphomas peculiar to Asia, such as adult T-cell leukemia/lymphoma and extranodal natural killer (NK)/T-cell lymphoma (ENKL), nasal type. References that provide scientific evidence for these guidelines have been selected by the Japanese Skin Cancer Society (JSCS) – Lymphoma Study Group. These guidelines, together with the degrees of recommendation, have been made in the context of limited medical treatment resources, and standard medical practice within the framework of the Japanese National Health Insurance system. The evidence level and degree of recommendation used for the current version are shown in Table 1.

## BASIS FOR THE CURRENT GUIDELINES

The cutaneous lymphomas listed in the present guidelines are basically in accordance with the WHO–EORTC classification (2005),[1] but it is difficult to precisely define "primary cutaneous" lymphoma. Ordinarily, a condition is defined as "primary cutaneous" lymphoma if appropriate procedures show no extracutaneous lesions at the time of diagnosis. The present guidelines include lymphomas and hematopoietic malignancies with marked affinity for the skin (Fig. 1, Table 2). The diagnostic nomenclature follows the 4th edition of the WHO classification (2008).[2]

To describe the skin lesions of cutaneous lymphoma, typically MF/SS, uniform terminology is needed. Without consistent terminology, accurate disease staging is impossible, and inconsistencies may develop in prognostic analysis. The ISCL/EORTC group has defined terminology for MF/SS.[9] Those definitions are adopted in the present guidelines (Table S1), and representative clinicopathological findings of various types of cutaneous lymphoma are provided in supporting information (Figs S1–S7).

## STAGING

### Staging for MF/SS (ISCL/EORTC 2007, modified in 2011)

For the staging of MF/SS, we previously used the categories developed by Bunn *et al.*[10] and Sausville *et al.*[11] In 2007, a new staging system was proposed by the ISCL/EORTC group,[3] which was modified in 2011 (Tables S2 and S3).[12]

In the ISCL/EORTC staging system, peripheral blood findings are classified into three categories: $B_0$ (atypical lymphocytes accounting for $\leq$5% of peripheral blood lymphocytes), $B_1$ (atypical lymphocytes accounting for >5% of peripheral blood lymphocytes, but <1000/μL), and $B_2$ (atypical lymphocyte

**Table 1.** Standards for the determination of evidence level and degree of recommendation

| | |
|---|---|
| Classification of evidence level | |
| I | Systematic review and/or meta-analysis<br>Staging/classification proposal and treatment recommendation or consensus paper from WHO, EORTC and ISCL |
| II | One or more randomized comparative studies |
| III | Non-randomized comparative studies |
| IV | Analytical epidemiology studies (cohort research and case–control studies)<br>Case series studies ($\geq$5 cases) |
| V | Descriptive studies (case reports and case series studies [<5 cases]) |
| VI | Opinions of expert committee and individual specialists* |
| Degree of recommendation classification† | |
| A | Strongly recommended for implementation (efficacy shown by at least 1 report providing level I or high-quality level II evidence) |
| B | Recommended for implementation (efficacy shown by $\geq$1 reports providing low-quality level II, high-quality level III, or very high-quality level IV evidence) |
| B-C1 | Recommended for implementation, but less strongly supported than B |
| C1 | Implementation can be considered, but evidence‡ is insufficient (low-quality III–IV, high-quality multiple V, or committee-approved VI evidence) |
| C2 | No evidence‡; cannot be recommended (no evidence of effectiveness, or evidence available of ineffectiveness) |
| D | Recommended not to implement (high-quality evidence of ineffectiveness or harmfulness) |

*Data from basic research and theories derived from such data are placed at this level. †Some of the "degree of recommendation" statements in these guidelines are not in complete agreement with the above table. ‡"Evidence" refers to knowledge from clinical trials and epidemiological research. This is because these "degree of recommendation" grades were based on a consensus among the committee members, taking feasibility into account. This consensus was reached after due consideration of the shortage of evidence internationally on the treatment of skin cancer and the fact that the evidence from overseas is not directly applicable in Japan.

 

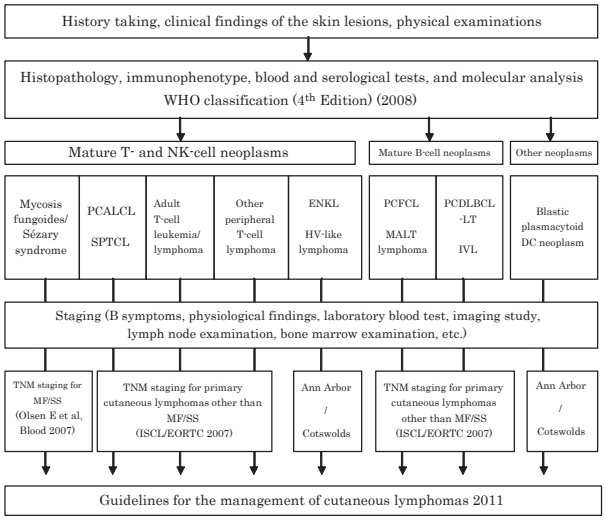


**Figure 1.** Diagnostic and staging algorithm for cutaneous lymphomas. DC, dendritic cell; ENKL, extranodal T/NK-cell lymphoma, nasal type; HV, hydroa vacciniforme; IVL, intravascular large B-cell lymphoma; MALT lymphoma, extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue type; MF/SS, mycosis fungoides/Sézary syndrome; PCALCL, primary cutaneous anaplastic large cell lymphoma; PCDLBCL-LT, primary cutaneous diffuse large B-cell lymphoma, leg type; PCFCL, primary cutaneous follicle center lymphoma; SPTCL, subcutaneous panniculitis-like T-cell lymphoma; TNM, tumor–node–metastasis; WHO, World Health Organization.

count of $\geq$1000/μL with a positive clone). Additional parameters that meet the $B_2$ criteria include the following: CD4/CD8 ratio of 10 or more, $CD4^+CD7^-$ of 40% or more, and $CD4^+CD26^-$ of 30% or more.[3,12,13] Cases with erythroderma who meet the $B_2$ criteria are defined as SS, or stage $IVA_1$ (Table S3 and Fig. S1). Erythrodermic MF of the $B_0$ or $B_1$ category is classified as stage IIIA or IIIB.

If lymphoma cells replace all or large portions of the lymph node structure, the condition is diagnosed as $N_3$ and is classified as stage $IV_2$ (Table S3). Even if the lymph node is infiltrated by atypical cells, a diagnosis of $N_3$ is not made as long as the foci are small and nodal architecture is preserved.[3,12]

### TNM classification of cutaneous lymphoma other than MF/SS (ISCL/EORTC 2007)

No TNM classification appropriate for the evaluation of cutaneous lesions was available for primary cutaneous lymphoma categories other than MF/SS. In 2007, the ISCL and EORTC proposed a new TNM classification system (Table S4).[4] Although the TNM classification reflect the extent of lesions, an adequate staging system has not been established yet. Moreover, the classification does not indicate prognoses for some disease types.[14] The category of "non-MF/SS" covers many types of cutaneous lymphoma, and new staging systems are needed for each disease type, based on the collected clinical data and prognostic analysis.

**Table 2.** Classification of cutaneous lymphomas

| |
|---|
| Cutaneous T/NK cell lymphoma |
| Mycosis fungoides: MF |
| Variants |
| Folliculotropic MF |
| Pagetoid reticulosis |
| Granulomatous slack skin |
| Sézary syndrome: SS |
| Adult T-cell leukemia/lymphoma |
| Primary cutaneous $CD30^+$ T-cell lymphoproliferative disorders |
| Primary cutaneous anaplastic large cell lymphoma |
| Lymphomatoid papulosis |
| Subcutaneous panniculitis-like T-cell lymphoma |
| Extranodal NK/T-cell lymphoma, nasal type |
| Hydroa vacciniforme-like lymphoma |
| Primary cutaneous γδ T-cell lymphoma |
| Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma* |
| Primary cutaneous $CD4^+$ small/medium T-cell lymphoma* |
| Peripheral T-cell lymphoma, not otherwise specified |
| Cutaneous B-cell lymphomas |
| Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue |
| Primary cutaneous follicle center lymphoma |
| Primary cutaneous diffuse large B-cell lymphoma, leg type |
| Intravascular large B-cell lymphoma |
| Hematological precursor cell neoplasm |
| Blastic plasmacytoid dendritic cell neoplasm |

*Provisional. Representative clinicopathological features of MF/SS, anaplastic large cell lymphoma, adult T-cell leukemia/lymphoma, subcutaneous panniculitis-like T-cell lymphoma, extranodal NK/T cell lymphoma, hydroa vacciniforme-like lymphoma, blastic plasmacytoid dendritic cell neoplasm have been shown in Figs S1–S7.

### Staging of other cutaneous lymphomas and hematopoietic malignancies

Shimoyama and colleagues have provided a widely-used classification of adult T-cell leukemia/lymphoma (ATLL): acute, lymphoma, chronic and smoldering types.[15] According to Shimoyama's criteria, ATLL patients with cutaneous lesions only are usually classified into the smoldering group. It is not appropriate to stage ATLL patients with the TNM system proposed by Kim *et al.*[4] because of the presence of minimal hematological disease. Furthermore, for other hematological malignancies such as ENKL, nasal type, and blastic plasmacytoid dendritic cell neoplasm, the Ann Arbor or Cotswolds staging (Table S5)[16] has been widely adopted in Japan because of hematological and extracutaneous spreading of the illness.

## EPIDEMIOLOGY OF CUTANEOUS LYMPHOMA

In line with the WHO classification (3rd edn), the incidence of all types of lymphomas was reported by pathologists in Japan.[17] The data were distinct from those in Western countries and similar in several ways to other data from Asia, although the relatively high rate of ATLL was attributed to the geographical difference in the etiologic factor, human T-lymphotropic virus

 

type 1 (HTLV-1). The JSCS – Lymphoma Study Group has conducted a nationwide survey of cutaneous lymphoma annually since 2007 (www.okayama-hihuka.jp/pdf/kekka2010.pdf). MF/SS account for approximately 51% of all cutaneous lymphomas, followed by ALCL and ATLL at approximately 9–8% each. B-cell lymphoma accounts for approximately 15% of all cutaneous lymphoma in Japan, so it is less frequent than in Europe or North America. ENLK, nasal type, accounts for only approximately 2%, which is nearly always associated with Epstein–Barr virus (EBV) infection. The NK-cell type is dominant in Japan.

## PROGNOSTIC ANALYSIS

Prognostic analyses of patients with cutaneous lymphoma are limited.[18–21] In the present guidelines, we have highlighted the prognoses of MF/SS, ATLL, and ENLK, nasal type, the latter two of which preferentially occur in Japan. For the other types of cutaneous lymphoma, we have used reports from other countries (Table 3).[22–26]

### MF/SS

Previous researchers already contributed to disease staging and prognostic analysis for MF/SS.[27] Since the new staging was advocated in 2007, prognostic analyses have been reported from Japan and the UK (Table 3).[18,22] The survival rates of Japanese patients with MF/SS were similar to those shown in previous studies conducted in the USA and Europe. The prognoses of patients with skin tumor (stage IIB) and extracutaneous involvement (stage IV) were significantly worse than those of patients with early-stage disease (stages IA–IIA). Erythrodermic MF patients without blood involvement (stage IIIA) showed excellent survival. Independent prognostic factors in multivariate analyses were higher age and the presence of either skin tumor or extracutaneous disease.[18] Although findings in Japan showed the prognosis for stage IIIA to be quite favorable, a British analysis indicated that it was similar to the prognosis for stage IIb,[22] this may have occurred because the two reports did not use the same diagnostic criteria for erythrodermic lymphoma, resulting in differences in patient characteristics.

### ATLL

A recent observation in Japan indicated that the patch and plaque types of ATLL were associated with better survival rates.[19] Multivariate analysis demonstrated that the hazard ratios of the erythrodermic and nodulotumoral types were significantly higher than that of the patch type, and that the eruption type is an independent prognostic factor for ATLL. The overall survival worsened as the T stage became more advanced: the multipapular type and T2 were comparable, and the purpuric type had a significantly poorer prognosis than T1 (Fig. S3).[19]

### ENKL

Suzuki *et al.*[20] have reported the prognosis of a total 150 patients with ENKL, nasal type, consisting of 123 nasal and 27 extranasal (16 cutaneous, nine hepatosplenic, one intestinal and one nodal) lymphomas. We focused on patients with the cutaneous type of ENKL, and re-examined their prognoses. Patients with stage I disease (determined by the Ann Arbor staging system) showed a favorable prognosis in 5-year overall survival of 75%, but the prognoses deteriorated in the advanced stages (Table 3). Unlike a previous study on $CD56^+$ hematological neoplasms with or without EBV infection in Europe,[28] our data highlighted that ENKL is usually associated with EBV infection, and assessed the prognoses of "nasal" and "cutaneous" ENKL separately.

## TREATMENT GUIDELINES

### Treatment guidelines for MF/SS

Mycosis fungoides/Sézary syndrome is the oldest defined form of cutaneous lymphoma, and is more common than other primary cutaneous lymphomas (Tables 4–11). At present, no treatment based on high-level evidence is available for this condition. In many cases, the clinical course may extend for 10 years or more. Therefore, the success or failure of therapeutic intervention may be difficult to determine. Moreover, ethical issues may complicate the implementation of randomized placebo-controlled studies. Only four randomized studies have compared the effectiveness of different treatment methods[29–32] and only one randomized placebo-controlled study has been conducted.[33] These guidelines give substantial weight to consensus among the committee members. The "B" recommendation level has been given to first-line therapies for daily clinical practice.

An additional problem is that far fewer treatment options are available for MF/SS in Japan than in Western countries. In the present guidelines, we have included information on treatment modalities that have not been approved by the Japanese National Health Insurance system. Experimental therapies not yet approved overseas or in Japan have been omitted from these guidelines.

CQ1: Is monitoring the clinical course without treatment recommended for MF?
Degree of recommendation: C1 (stage IA only), C2 (other than stage IA).
Recommendation: In stage IA of MF, one acceptable option is to monitor the clinical course without treatment. For stages beyond IA, monitoring the clinical course without treatment is generally not recommended (Data S1).

CQ2: Are topical steroids recommended for MF/SS?
Degree of recommendation: B.
Recommendation: Topical steroid therapy is recommended at all stages of MF/SS (Data S1).

CQ3: Is topical chemotherapy recommended for MF/SS?
Degree of recommendation: C1.
Recommendation: Mechlorethamine/nitrogen mustard (HN2) or carmustine (BCNU) topical chemotherapy is currently used in Europe and North America, and is recommended for early-stage MF (stage IA through IIA). These agents are not yet approved or available in Japan. Nimustine hydrochloride (ACNU) is currently used topically in some facilities in Japan,

**Table 3.** Survival rates of various cutaneous lymphomas and hematological neoplasms

| Disease | Stage | 5y-OS | 5y-DSS | Median survival time (months) | References |
|---|---|---|---|---|---|
| MF/SS | IA | 94–100 | 98–100 | 426 | 18, 22 |
| | IB | 84–89 | 89–95 | 258 | |
| | IIA | 78–87 | 87–89 | 190 | |
| | IIB | 47–73 | 56–88 | 56–78 | |
| | IIIA | 47–100 | 54–100 | 56 | |
| | IIIB | 40 | 48 | 41 | |
| | IVA1 | 0–37 | 0–41 | 23–46 | |
| | IVA2 | 18–33 | 23–50 | 25–46 | |
| | IVB | 0–18 | 0–18 | 13–17 | |
| ATLL | T1 | 82.5 | 82.5 | 192.6* | 19, 23 |
| | T2 | 27.3 | 27.3 | 47.9 | |
| | T3 | 0 | 0 | 17.3 | |
| | T4 | 0 | 0 | 3 | |
| | Multi-papular type | 42.1 | 47.1 | | |
| | Purpuric type | 40.0 | 40.0 | | |
| ALCL | T1 | 85 | 93 | | 24 |
| | T2 | 81 | 93 | | |
| | T3 | 63 | 77 | | |
| | Leg (–) | 86 | 100 | | |
| | Leg (+) | 53 | 67 | | |
| SPTCL | HPS (–) | 91 | | | 25 |
| | HPS (+) | 45 | | | |
| | | Total 82 | | | |
| Nasal ENKL | I | 55 (4 years) | | 59.8 | 20 |
| | II | 33 (4 years) | | 11.2 | |
| | III | 31 (4 years) | | 33.1 | |
| | IV | 10 (4 years) | | 5.3 | |
| | | Total 36 (4 years) | | Total 12.9 | |
| Cutaneous extranasal ENKL | I | 75 (2 years) | | Not reached | 20 |
| | II | 0 (2 years) | | 6.2 | |
| | III | Not reached† | | 75.5† | |
| | IV | 14 (2 years) | | 4 | |
| | | Total 33 (2 years) | | Total 6.8 | |
| BNKL | BM/blood (–) | 0 | 25.3 (2 years) | 17.1 | 21 |
| | BM/blood (+) | 19.6 | 46.4 (2 years) | 20.4 | |
| | Skin (–) | 0 | 21 (2 years) | 24.2 | |
| | Skin (+) | 20 | 48 (2 years) | 22.2 | |
| Extranodal MZL of MALT | | 94–97 | | | 26, 27 |
| PCFCL | | 87–96 | | | |
| PCDLBCL | | 37–73 | | | |

*Mean survival time. †One case. ALCL, anaplastic large cell lymphoma; ATLL, adult T cell leukemia/lymphoma; BM, bone marrow; BNKL, blastic NK-cell lymphoma; DSS, disease-specific survival; ENKL, extranodal NK/T-cell lymphoma; HPS, hemophagocytic syndrome; MF, mycosis fungoides; MZL of MALT, marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue; OS, overall survival; PCDLBCL, primary cutaneous diffuse large B-cell lymphoma; PCFCL, primary cutaneous follicle center lymphoma; SPTCL, subcutaneous panniculitis-like T-cell lymphoma; SS, Sezary syndrome.

and can be considered for small skin lesions or for short-term use (Data S1).

CQ4: Is ultraviolet (UV) light therapy recommended for MF/SS?
Degree of recommendation: B.
Recommendation: Oral psoralen plus UV-A therapy (PUVA) therapy or narrow-band UV-B therapy is recommended for early-stage MF (stage IA through IIA) (Data S1).

CQ5: Is PUVA therapy with concomitant retinoid or interferon (IFN) therapy recommended for MF/SS?
Degree of recommendation: B.
Recommendation: PUVA with concomitant oral etretinate (RePUVA) or PUVA with concomitant IFN is recommended for MF/SS (Data S1).

CQ6: Is radiation therapy recommended for MF/SS?
Degree of recommendation: B.
Recommendation: Localized radiation therapy is recommended as a palliative treatment for skin lesions in MF, regardless of disease stage. Total skin electron beam therapy is recommended for MF (stage IB through IIA) (Data S1).

CQ7: Are oral retinoids recommended for MF/SS?
Degree of recommendation: B-C1.

 

**Table 4.** Summary of clinical questions and degree of recommendation for mycosis fungoides/Sézary syndrome

| Clinical question | Degree of recommendation |
|---|---|
| CQ1: Is monitoring the clinical course without treatment recommended for mycosis fungoides? | C1 (stage IA)<br>C2 (other than stage IA) |
| CQ2: Are topical steroids recommended for mycosis fungoides/Sézary syndrome? | B |
| CQ3: Is topical chemotherapy recommended for mycosis fungoides/Sézary syndrome? | C1 |
| CQ4: Is ultraviolet light therapy recommended for mycosis fungoides/Sézary syndrome? | B |
| CQ5: Is psoralen plus ultraviolet A therapy with concomitant retinoid or interferon therapy recommended for mycosis fungoides/Sézary syndrome? | B |
| CQ6: Is radiation therapy recommended for mycosis fungoides/Sézary syndrome? | B |
| CQ7: Are oral retinoids recommended for mycosis fungoides/Sézary syndrome? | B-C1 |
| CQ8: Is interferon therapy recommended for mycosis fungoides/Sézary syndrome? | B-C1 |
| CQ9: Is extracorporeal photochemotherapy recommended for mycosis fungoides/Sézary syndrome? | B (erythroderma)<br>C1 (non-erythroderma) |
| CQ10: Are molecular-targeted therapies recommended for mycosis fungoides/Sézary syndrome? | B-C1 |
| CQ11: Is chemotherapy recommended for mycosis fungoides/Sézary syndrome? | B (refractory, extracutaneous lesions)<br>D (early stage) |
| CQ12: Is hematopoietic stem cell transplantation recommended for mycosis fungoides/Sézary syndrome? | C1 (allogeneic)<br>C2 (autologous) |

**Table 5.** (MF/SS-1) Topical therapy of first choice recommended for stages I and IIA*

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| Monitoring the clinical course without treatment | C1 (stage IA only)/C2 | CQ1 |
| Topical steroid therapy† | B | CQ2 |
| ACNU topical therapy‡ | C1 | CQ3 |
| BB-UVB† | B | CQ4 |
| NB-UVB | B | CQ4 |
| PUVA | B | CQ4 |
| Localized radiation therapy§ | B | CQ6 |

*If the patient does not respond to the topical therapy selected for initial treatment, before proceeding to a second-line therapy recommended for stage I through IIA (Table 6 MFSS-2), consider the use of other first-line topical therapies. †Stage IA/IB. ‡Small area, short-term use. §Radical radiation therapy for "minimal" stage IA unilesional mycosis fungoides, or where multiple lesions are localized within the same radiation field or multiple field in close proximity, and palliative radiation for infiltrated plaques resistant to topical therapy other than radiation. ACNU, nimustine hydrochloride; BB, broad-band; NB, narrowband; PUVA, psoralen plus ultraviolet A therapy; UVB, ultraviolet B.

**Table 6.** (MF/SS-2) Second-line therapy recommended for stages I and IIA

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| TSEB* | B | CQ6 |
| Etretinate†,‡ | B-C1 | CQ7 |
| IFN-α†,§ | B-C1 | CQ8 |
| IFN-γ† | B-C1 | CQ8 |
| RePUVA† | B | CQ5 |
| IFN-α + PUVA †,§ | B | CQ5 |
| IFN-γ + PUVA † | B | CQ5 |
| Chemotherapy¶ | D/B¶ | CQ11 |

*TSEB can be used as first-line therapy for stage IB/IIA (T2) with intense subjective symptoms accompanied by extensive highly infiltrated plaques and histopathological confirmation of folliculotropic mycosis fungoides or large cell transformation. †Can be a first-line treatment if systemic therapy is required (B1 or histopathological confirmation of folliculotropic mycosis fungoides or large cell transformation). BRM therapy (etretinate, IFN-α, IFN-γ) can be used as monotherapy or in concomitant administration with PUVA, and its concomitant use can also be investigated with topical therapies other than PUVA. ‡Duration of response to oral etretinate is usually short; consider for use as concomitant therapy. §IFN-α therapy has been used in only a few cases in Japan. ¶Third-line therapy for stage IB/IIA disease resistant to skin-targeted therapy and BRM therapy. BRM, biological response modifiers; IFN, interferon; PUVA, psoralen plus ultraviolet A therapy; TSEB, total skin electron beam.

Recommendation: Oral etretinate can be useful in the treatment of MF/SS (Data S1).

CQ8: Is IFN therapy recommended for MF/SS?
Degree of recommendation: B-C1.

Recommendation: IFN-α therapy is recommended in early-stage MF/SS (stage IA–IIA) if systemic therapy is required, and in advanced disease (stage IIB–IVA1). This treatment option has not yet been approved in Japan. IFN-γ, which has been used for the treatment of MF in Japan, is considered as effective as IFN-α, and may prove useful (Data S1).

CQ9: Is extracorporeal photochemotherapy (ECP) recommended for MF/SS?
Degree of recommendation: B (erythrodermic MF/SS), C1 (non-erythrodermic disease).

Recommendation: ECP/photopheresis is recommended for stage T4 erythrodermic MF and SS. It may also be considered in cases of refractory non-erythrodermic MF. ECP is

**Table 7.** (MF/SS-3) First-line therapy recommended for stage IIB*

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| Concomitant use of the following forms of BRM therapy and topical therapy | | |
| BRM therapy | | |
| Etretinate | B-C1 | CQ5,7 |
| IFN-α†,‡ | B-C1 | CQ5,8 |
| IFN-γ‡ | B-C1 | CQ5,8 |
| Topical therapy | | |
| PUVA ± localized radiation therapy§ | B | CQ4,5,6 |
| Localized radiation therapy§ | B | CQ6 |
| TSEB¶ | B | CQ6 |

*If the patient does not respond to initial treatment, before proceeding to a second-line therapy recommended for refractory stage IIB (Table 8 MFSS-4), consider other first-line topical therapies. †Concomitant therapy with IFN-α and PUVA: degree of recommendation = B. IFN-α therapy has been used in only a few cases in Japan. ‡IFN-α monotherapy or IFN-γ monotherapy can be used as first-line therapy. §Palliative radiation for localized tumors. ¶If lesions extend over <10% of body surface area, TSEB monotherapy can be used as first-line therapy. BRM, biological response modifiers; IFN, interferon; PUVA, psoralen plus ultraviolet A therapy; TSEB, total skin electron beam.

**Table 8.** (MF/SS-4) Treatment methods recommended for refractory stage IIB/III or stage IV mycosis fungoides

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| Chemotherapy* | B | CQ11 |

*Consider concomitant use of topical therapy appropriate for T classification.

**Table 9.** (MF/SS-5) First-line therapy recommended for stage III *

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| ECP ± IFN-α† | B | CQ9 |
| TSEB + ECP†,‡ | B | CQ6 |
| Concomitant use of the following forms of BRM therapy and topical therapy | | |
| BRM therapy | | |
| Etretinate | B-C1 | CQ5,7 |
| IFN-α†,§ | B-C1 | CQ5,8 |
| IFN-γ§ | B-C1 | CQ5,8 |
| Topical therapy | | |
| PUVA | B | CQ4,5 |
| TSEB§ | B | CQ6 |

*If the patient does not respond to initial therapy, before proceeding to a therapy recommended for refractory stage III (Table 8 MFSS-4), consider other first-line therapies. †ECP and IFN-α therapy have been used in only a few cases in Japan. ‡TSEB monotherapy can be used as first-line therapy for stage IIIA disease. §IFN-α monotherapy or IFN-γ monotherapy can be used as first-line therapy. BRM, biological response modifiers; ECP, Extracorporeal photochemotherapy; IFN, interferon; PUVA, psoralen plus ultraviolet A therapy; TSEB, total skin electron beam.

**Table 10.** (MF/SS-6) Recommended therapy for Sézary syndrome (stage T4, IVA1-IVB)*

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| ECP ± IFN-α† | B | CQ9 |
| TSEB + ECP† | B | CQ6 |
| Chemotherapy ± IFN-α† | B | CQ11 |

*For stage IVA1 Sézary syndrome with a low Sézary cell count, initial therapy selection may be the same as for stage IIIB (Table 9 MF/SS-5). †ECP and IFN-α therapy have been used in only a few cases in Japan. ECP, extracorporeal photochemotherapy; IFN, interferon; TSEB, total skin electron beam.

**Table 11.** (MF/SS-7) Treatment to be considered for refractory stage IV disease

| Treatment | Degree of recommendation | CQ |
|---|---|---|
| Allogeneic hematopoietic stem cell transplantation | C1 | CQ12 |
| Autologous hematopoietic stem cell transplantation | C2 | CQ12 |

not yet approved by the Japanese National Health Insurance system, and currently almost no Japanese medical institutions perform the procedure (Data S1).

CQ10: Are molecular-targeted therapies recommended for MF/SS?
Degree of recommendation: B-C1.
Recommendation: Treatment with denileukin diftitox, vorinostat or romidepsin may be useful in recurrent or refractory MF/SS. Vorinostat is the only drug in this category that is approved for coverage by Japanese health insurance (Data S1).

CQ11: Is chemotherapy recommended for MF/SS?
Degree of recommendation: B (if disease is refractory or accompanied by extracutaneous lesions), D (early-stage MF).
Recommendation: Chemotherapy is not recommended as a first line of treatment in early-stage MF (stage IA–IIA). Chemotherapy is recommended for MF/SS stage IB–IIIB that is resistant to topical therapy or biological response modifier therapy, and for MF/SS stage IVA1–IVB accompanied by extracutaneous lesions (Data S1).

CQ12: Is hematopoietic stem cell transplantation recommended for MF/SS?
Degree of recommendation: C1 (allogeneic hematopoietic stem cell transplantation), C2 (autologous hematopoietic stem cell transplantation).
Recommendation: Autologous hematopoietic stem cell transplantation with concomitant high-dose chemotherapy is not generally recommended for MF/SS. In young patients with advanced disease, allogeneic hematopoietic stem cell transplantation may be considered in the context of a clinical study (Data S1).

## Cutaneous T/NK-cell lymphoma other than MF/SS (non-MF/SS)

Cutaneous T/NK cell lymphomas other than MF/SS are classified by WHO–EORTC into two broad categories: relatively aggressive lymphomas with poor prognosis (aggressive group), and indolent lymphomas with favorable prognosis (indolent group) (Table 12).[1,34–39] In patients with aggressive lymphomas including primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma, primary cutaneous $\gamma\delta$ T-cell lymphoma, and peripheral T-cell lymphoma, not otherwise specified, the 5-year survival rates are less than 20%. However, the clinical course is not uniform, and patients whose symptoms are limited to cutaneous lesions may live for much longer.

For patients who present with cutaneous lesions only, without general symptoms or notable laboratory test findings, skin-directed therapies used for MF/SS might be chosen as a first-line treatment. Systemic chemotherapy may be considered for patients with tumor infiltration into the lymph nodes or visceral organs. However, the best treatment option must be explored for each individual patient, based on that patient's conditions. Clinical questions (CQ) are not defined in this category because uniform guidelines are difficult to develop. In contrast, CQ have been defined in each lymphoma in the indolent group (primary cutaneous anaplastic large cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, and primary cutaneous $CD4^+$ small/medium T-cell lymphoma).

The MF/SS staging classifications are not applicable to cutaneous T/NK cell lymphomas other than MF/SS because of differences in disease progression. In 2007, the ISCL and EORTC jointly advocated the TNM classification system for cutaneous lymphomas other than MF/SS.[4] Because the prognostic impact of this classification system has not yet been validated, it might be premature to establish guidelines based on it. However, no other applicable classification systems are available at the present time. In order to obtain clinical information based on common criteria, we have adopted the TNM classification in the present guidelines.

*Primary cutaneous anaplastic large cell lymphoma.*

CQ13: Are localized therapies such as radiation therapy or surgical resection recommended for primary cutaneous anaplastic large cell lymphoma?
Degree of recommendation: B.
Recommendation: Remission can be induced by radiation therapy or surgical resection in many patients, so these methods are recommended where feasible (Data S1).

CQ14: Is chemotherapy recommended for primary cutaneous anaplastic large cell lymphoma?
Degree of recommendation: B (for lymph node lesions and visceral organ infiltration), C1 (symptoms limited to cutaneous lesions only).
Recommendation: For patients with cutaneous lesions only, if those lesions are resistant to topical treatment such as radiotherapy and surgical excision, or if they have multiple lesions, chemotherapy may be considered. Chemotherapy is recommended for lymph node lesions and for infiltration in the visceral organs (Data S1).

*Subcutaneous panniculitis-like T-cell lymphoma.*

CQ15: Is radiation therapy recommended for subcutaneous panniculitis-like T-cell lymphoma?
Degree of recommendation: C1.
Recommendation: Radiation therapy can provide control of localized lesions within the irradiated area. Radiation can be considered as initial therapy for skin lesions within a localized area (T1, T2) without systemic symptoms (Data S1).

CQ16: Are oral steroids recommended for subcutaneous panniculitis-like T-cell lymphoma?
Degree of recommendation: B.
Recommendation: Steroid monotherapy has been reported to relieve systemic symptoms such as pyrexia and abnormal hepatic function and to induce remission in some cases; oral steroids are recommended for subcutaneous panniculitis-like T-cell lymphoma (Data S1).

**Table 12.** Summary of CQ and degree of recommendation for cutaneous T-/natural killer cell lymphoma (non-MF/SS)

| Clinical question | Degree of recommendation |
|---|---|
| CQ13: Are localized therapies such as radiation therapy B or surgical resection recommended for primary cutaneous anaplastic large cell lymphoma? | B |
| CQ14: Is chemotherapy recommended for primary cutaneous anaplastic large cell lymphoma? | B (extracutaneous lesions)<br>C1 (cutaneous lesions only) |
| CQ15: Is radiation therapy recommended for subcutaneous panniculitis-like T-cell lymphoma? | C1 |
| CQ16: Are oral steroids recommended for subcutaneous panniculitis-like T-cell lymphoma? | B |
| CQ17: Is combination chemotherapy recommended for subcutaneous panniculitis-like T-cell lymphoma? | B-C1 |
| CQ18: Is radiation therapy recommended for primary cutaneous $CD4^+$ small/medium T-cell lymphoma? | B |
| CQ19: Is chemotherapy recommended for primary cutaneous $CD4^+$ small/medium T-cell lymphoma? | C1 |

CQ17: Is combination chemotherapy recommended for subcutaneous panniculitis-like T-cell lymphoma?
Degree of recommendation: B-C1.
Recommendation: Combination chemotherapy may be considered if the condition is resistant to steroid therapy. Prognosis is poor for patients complicated by hemophagocytosis; combination chemotherapy is recommended in such cases (Data S1).

*Primary cutaneous CD4$^+$ small/medium T-cell lymphoma.*

CQ18: Is radiation therapy recommended for primary cutaneous CD4$^+$ small/medium T-cell lymphoma?
Degree of recommendation: B.
Recommendation: Radiation therapy can induce remission in many cases, and survival rates are relatively good. Radiation therapy is recommended for single and localized lesions (T1, T2) (Data S1).

CQ19: Is chemotherapy recommended for primary cutaneous CD4$^+$ small/medium T-cell lymphoma?
Degree of recommendation: C1.
Recommendation: Chemotherapy can also be considered for primary cutaneous CD4$^+$ small/medium T-cell lymphoma with multiple lesions (Data S1).

### ATLL (disease type limited to cutaneous lesions)

Adult T-cell leukemia/lymphoma is a form of T-cell lymphoma caused by HTLV-1 which occurs in a variety of organs (Table 13). Three major findings required for diagnosis: (i) appearance of morphologically abnormal T lymphocytes (typically CD4$^+$ and CD25$^+$); (ii) seropositivity for anti-HTLV-1 antibody; and (iii) Southern blot confirmation for monoclonal integration of HTLV-1 provirus into tumor cells.[15,40] For cutaneous symptoms to be diagnosed as eruptions specific to ATLL, histological confirmation is required for (i) and (iii). In particular, (iii) is required for a differential diagnosis to exclude other cutaneous lymphomas such as MF. The overall treatment guidelines for ATLL must involve cooperation and coordination with other departments, including departments of hematology and oncology. Thus, we limit these guidelines to instances in which only cutaneous lesions are detected. However, no uniform diagnostic criteria exist for the conventionally advocated concept of "cutaneous" ATLL.[40–43] The present guidelines cover ATLL cases, where systemic treatments such as chemotherapy and transplantation are not indicated.

**Table 13.** Summary of CQ and degree of recommendation for adult T-cell leukemia/lymphoma (ATLL) with cutaneous lesions only

| Clinical question | Degree of recommendation |
|---|---|
| CQ20: Is ultraviolet light therapy recommended for ATLL with cutaneous lesions only? | B-C1 |
| CQ21: Is radiation therapy recommended for ATLL with cutaneous lesions only? | B |
| CQ22: Are oral retinoids recommended for ATLL with cutaneous lesions only? | C1 |
| CQ23: Is interferon therapy recommended for ATLL with cutaneous lesions only? | C1 |
| CQ24: Is single-agent chemotherapy recommended for ATLL with cutaneous lesions only? | B-C1 |

Eruptions specific to ATLL are defined as cutaneous symptoms in cases seropositive for anti-HTLV-1 antibody and where cutaneous histology shows monoclonal integration of HTLV-1. In the present guidelines, we have provisionally considered "ATLL with cutaneous lesions only" to be "cases in which ATLL cells account for <5% of all peripheral blood cells, excluding the acute, lymphoma, and chronic types".[19,40]

CQ20: Is UV light therapy recommended for ATLL with cutaneous lesions only?
Degree of recommendation: B-C1.
Recommendation: PUVA therapy can induce remission in ATLL with cutaneous lesions only, and may be useful. Regardless of whether extracutaneous lesions are present, PUVA can be expected to relieve cutaneous symptoms. However, beneficial effects of PUVA on extracutaneous lesions or the prognosis of patients have not been confirmed (Data S1).

CQ21: Is radiation therapy recommended for ATLL with cutaneous lesions only?
Degree of recommendation: B.
Recommendation: Radiation therapy can be expected to provide symptomatic relief in ATLL with cutaneous lesions only, and is recommended. However, beneficial effects on the prognosis of patients have not been confirmed (Data S1).

CQ22: Are oral retinoids recommended for ATLL with cutaneous lesions only?
Degree of recommendation: C1.
Recommendation: Retinoids can induce remission in ATLL with cutaneous lesions only, and may be considered for use (Data S1).

CQ23: Is IFN therapy recommended for ATLL with cutaneous lesions only?
Degree of recommendation: C1.
Recommendation: IFN-$\gamma$ can relieve symptoms in ATLL with cutaneous lesions only, and may be considered for use. Beneficial effects on extracutaneous lesions or the prognosis of patients have not been confirmed (Data S1).

CQ24: Is single-agent chemotherapy recommended for ATLL with cutaneous lesions only?
Degree of recommendation: B-C1.
Recommendation: Single-agent chemotherapy can be useful for disease refractory to skin-direct therapy in cases where combination chemotherapy is not indicated. However, beneficial effects on the prognosis of patients have not been confirmed (Data S1).

### Other T/NK-cell lymphomas

In addition to ENKL, the WHO classification for hematopoietic malignancies, revised in 2008, has listed hydroa

vacciniforme-like lymphoma as an independent disease (Table 14).[2] This condition has been reported in Asia, including Japan, in Mexico, and in Peru. Hydroa vacciniforme-like lymphoma is a form of T-cell lymphoma that is associated with EBV. It occurs most frequently in children and adolescents, and is often accompanied by photosensitivity and hypersensitivity to insect bites. Prognosis, although varied, is poor if complicated by systemic conditions such as hemophagocytosis. There have been no reports of treatment for this condition alone, but a few reports are available on treatment of chronic active EBV infection and on $EBV^+$ T/NK-cell lymphoproliferative diseases. Treatment has been attempted with antiviral therapy using the antiviral agents acyclovir and ganciclovir, immunotherapy using agents such as IFN-$\alpha$ and interleukin 2, and chemotherapy using corticosteroids and etoposide.[44] However, the reports involve a very small number of cases, insufficient even for descriptive research, so findings cannot be considered conclusive.

Blastic plasmacytoid dendritic cell neoplasm is a rare disease formerly designated as $CD4^+/CD56^+$ hematodermic neoplasm.[45] Most patients usually respond to initial polychemotherapy, but the relapse rate is high. The prognosis is dismal, with a median overall survival of 12–14 months.

*ENKL, nasal type.*

CQ25: Is CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) chemotherapy recommended for ENKL, nasal type?

Degree of recommendation: C2.

Recommendation: ENKL, nasal type, generally responds poorly or only temporarily to CHOP therapy; this treatment is not recommended (Data S1).

CQ26: Is combination radiation therapy and chemotherapy recommended for ENKL, nasal type?

Degree of recommendation: B.

Recommendation: For localized lesions, radiation therapy with simultaneous or subsequent DeVIC (dexamethasone, VP16, ifosfamide, carboplatin) chemotherapy is recommended (Data S1).

*Blastic plasmacytoid dendritic cell neoplasm.*

CQ27: Is chemotherapy recommended for blastic plasmacytoid dendritic cell neoplasm?

Degree of recommendation: C1.

Recommendation: No standard treatment has been established for blastic plasmacytoid dendritic cell neoplasm. Multidrug chemotherapy may be considered. However, such treatment provides only temporary effectiveness, and almost all patients die within a few years (Data S1).

*Hydroa vacciniforme-like lymphoma.*

CQ28: Is allogenic hematopoietic stem cell transplantation recommended for hydroa vacciniforme-like lymphoma?

Degree of recommendation: B-C1.

Recommendation: Allogenic hematopoietic stem cell transplantation may be useful in the treatment of hydroa vacciniforme-like lymphoma (Data S1).

## Cutaneous B-cell lymphoma

The WHO–EORTC classification of 2005 lists the following subtypes within the category of cutaneous B-cell lymphoma:[1] primary cutaneous marginal zone B-cell lymphoma (PCMZL); primary cutaneous follicle center cell lymphoma (PCFCL), primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL, leg type); PCLBCL, other; and intravascular large B-cell lymphoma (IVL) (Table 15). In the 2008 revision of the WHO classification of hematopoietic malignancies, the nomenclature, the PCMZL was replaced by "extranodular marginal zone B-cell lymphoma (MALT lymphoma)".[2] The term, PCDLBCL, leg type, was entered as a subcategory of "diffuse large B-cell lymphoma, not otherwise specified". The term "primary cutaneous diffuse large B-cell lymphoma, other" was removed from the list. Disease type is an important prognostic factor for cutaneous B-cell lymphoma. Both PCFCL and PCMZL are indolent-type lymphomas with a favorable prognosis, while prognosis is poor in PCDLBCL and IVL. In the following discussion, cutaneous B-cell lymphoma is divided into two groups: the indolent group and diffuse large cell group.

No randomized clinical trials have been conducted in these disease groups, and research has been limited primarily to descriptive studies. However, in 2008, the EORTC and ISCL published guidelines for the treatments of cutaneous B-cell lymphoma, based on previous reports.[46] Most of the reported treatment methods for topical therapy involved radiation and/or surgical resection. Most of the methods for systemic therapy involved chemotherapy and the administration of rituximab. However, a few reports were found on topical administration of IFN-$\alpha$ and on the use of photodynamic therapy.

**Table 14.** Summary of CQ and degree of recommendation for other natural killer (NK)/T-cell lymphomas and related diseases

| Clinical question | Degree of recommendation |
|---|---|
| CQ25: Is CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) chemotherapy recommended for extranodal NK/T-cell lymphoma, nasal type? | C2 |
| CQ26: Is combination radiation therapy and chemotherapy recommended for extranodal NK/T-cell lymphoma, nasal type? | B |
| CQ27: Is chemotherapy recommended for blastic plasmacytoid dendritic cell neoplasm? | C1 |
| CQ28: Is allogenic stem cell transplantation recommended for hydroa vacciniforme-like lymphoma? | B-C1 |

 

**Table 15.** Summary of CQ and degree of recommendation for primary cutaneous B-cell lymphoma (indolent type: primary cutaneous follicle center lymphoma and extranodal marginal zone lymphoma)

| Clinical question | Degree of recommendation |
|---|---|
| CQ29: Is radiation therapy recommended for indolent-type primary cutaneous B-cell lymphoma? | B |
| CQ30: Is surgical resection recommended for indolent-type primary cutaneous B-cell lymphoma? | B |
| CQ31: Is rituximab monotherapy recommended for indolent-type primary cutaneous B-cell lymphoma? | B-C1 |
| CQ32: Is combination chemotherapy recommended for indolent-type primary cutaneous B-cell lymphoma? | C1 |
| CQ33: Is combination chemotherapy recommended for primary cutaneous diffuse large B-cell lymphoma? | B |
| CQ34: Is rituximab monotherapy recommended for primary cutaneous diffuse large B-cell lymphoma? | B |
| CQ35: Are surgical resection and radiation therapy recommended for diffuse large B-cell lymphoma? | C1 |

CQ29: Is radiation therapy recommended for indolent-type primary cutaneous B-cell lymphoma?
Degree of recommendation: B.
Recommendation: Radiotherapy is recommended for diseases in the indolent group (PCMZL and PCFCL) (Data S1).

CQ30: Is surgical resection recommended for indolent-type primary cutaneous B-cell lymphoma?
Degree of recommendation: B.
Recommendation: Surgical resection is recommended for resectable lesions of diseases in the indolent group (PCMZL and PCFCL) (Data S1).

CQ31: Is rituximab monotherapy recommended for indolent-type primary cutaneous B-cell lymphoma?
Degree of recommendation: B-C1.
Recommendation: Rituximab may be useful for the treatment of diseases in the indolent group (PCMZL and PCFCL), particularly in cases of multiple lesions (Data S1).

CQ32: Is combination chemotherapy recommended for indolent-type primary cutaneous B-cell lymphoma?
Degree of recommendation: C1.
Recommendation: Combination chemotherapy may be considered for diseases in the indolent group that are refractory to other treatment regimens, and for advanced extracutaneous disease (Data S1).

CQ33: Is combination chemotherapy recommended for PCDLBCL?
Degree of recommendation: B.
Recommendation: Combination chemotherapy, and particularly the concomitant use of rituximab, is recommended for PCDLBCL, leg type, and for IVL (Data S1).

CQ34: Is rituximab monotherapy recommended for PCDLBCL?
Degree of recommendation: B.
Recommendation: Rituximab monotherapy is recommended for the treatment of PCDLBCL in cases where combination therapy may be poorly tolerated, such as in the elderly and in patients with severe complications (Data S1).

CQ35 Are surgical resection and radiation therapy recommended for PCDLBCL?
Degree of recommendation: C1.
Recommendation: In patients who cannot tolerate rituximab combination chemotherapy, such as the elderly and patients with severe complications, surgical resection and radiation therapy may be considered (Data S1).

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Data S1.** References used for treatment recommendations (CQ1–CQ35).

**Table S1.** Terminology for clinical features of mycosis fungoides/Sézary syndrome.

**Table S2.** Tumor, lymph nodes, metastasis, blood (TNMB) classification for mycosis fungoides/Sézary syndrome.

**Table S3.** TNMB staging for mycosis fungoides/Sézary syndrome (International Society for Cutaneous Lymphomas/European Organization for Research and Treatment of Cancer, Cutaneous Lymphomas Task Force).

**Table S4.** Tumor–node–metastasis classification for primary cutaneous lymphomas other than mycosis fungoides/Sézary syndrome.

**Table S5.** Ann Arbor/Cotswold staging.

**Figure S1.** Clinicopathological features of mycosis fungoides/Sézary syndrome.

**Figure S2.** Clinical features of anaplastic large cell lymphoma.

**Figure S3.** Clinical features of adult T-cell leukemia/lymphoma.

**Figure S4.** Clinicopathological features of subcutaneous panniculitis-like T-cell lymphoma.

**Figure S5.** Clinical features of extranodal natural killer/T-cell lymphoma, nasal type.

**Figure S6.** Clinicopathological features of hydroa vacciniforme-like lymphoma.

**Figure S7.** Clinical features of blastic plasmacytoid dendritic cell neoplasm.

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