JAMA | Review

Classic Hodgkin Lymphoma
A Review

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IMPORTANCE Hodgkin lymphoma (HL) is a lymphoid malignancy derived from B cells. Globally, there were 82 409 new cases of HL in 2022, associated with 22 701 deaths. In the US, 8720 incident cases of HL and 1150 deaths due to HL were reported in 2025. Classic HL (cHL) accounts for 90% to 95% of HL cases.

OBSERVATIONS Classic HL has a bimodal age distribution, with an initial peak at age 15 to 35 years and a second, smaller peak at approximately age 70 years. The median age at cHL diagnosis is 33 years. Most patients present with supradiaphragmatic lymphadenopathy (cervical, mediastinal, supraclavicular, or axillary lymph node involvement or a combination of these lymph nodes); isolated infradiaphragmatic involvement occurs in less than 10% of individuals. Approximately 30% to 40% of patients have B (systemic) symptoms, including fevers (>38.3 °C), drenching sweats, and unintentional weight loss (>10% of body weight during the prior 6 months). Risk factors for cHL include Epstein-Barr virus infection, immune dysregulation (autoimmunity or immunosuppression), and familial predisposition. Patients with early-stage cHL (stage I-II) are risk stratified based on presence of favorable or unfavorable features, which include older age, elevated erythrocyte sedimentation rate, B symptoms, higher disease bulk (>10 cm for a nodal mass or greater than one-third of the internal transverse thoracic diameter at T5 to T6 for a mediastinal mass, measured on chest radiograph), increased number of nodal sites, and extranodal involvement. Patients with early-stage cHL receive chemotherapy with or without consolidative radiotherapy; advanced-stage disease (stage III-IV) is typically treated with chemotherapy alone. Novel agents, including anti–programmed cell death 1 immunotherapy or the CD30-targeted antibody-drug conjugate brentuximab vedotin, are combined with chemotherapy for some patients with early-stage unfavorable cHL and all patients with advanced-stage cHL. Patients with relapsed or refractory cHL who meet eligibility criteria should undergo high-dose chemotherapy and autologous stem cell transplant, with curative intent. Allogeneic stem cell transplant is reserved for select patients with relapse after high-dose chemotherapy and autologous stem cell transplant. Cure is achieved in up to 90% of treated patients with both early-stage and advanced-stage disease. However, survivors have increased risk of secondary malignancies (including non-Hodgkin lymphomas; breast, lung, and colorectal cancers; and myelodysplasia), cardiopulmonary dysfunction, and thyroid dysfunction.

CONCLUSIONS AND RELEVANCE First-line treatment for cHL is chemotherapy, with addition of radiotherapy for some patients with early-stage disease. Select patients with unfavorable early-stage cHL and all patients with advanced-stage cHL should also receive anti–programmed cell death 1 immunotherapy or a CD30-targeted antibody-drug conjugate in addition to chemotherapy. Patients with relapsed or refractory cHL should be evaluated for stem cell transplant.

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Hodgkin lymphoma (HL) is a relatively rare disease; globally, there were 82 409 incident cases reported in 2022, associated with 22 701 deaths and accounting for approximately 13% of all lymphoma diagnoses and 0.4% of all cancers.[1] Classic HL (cHL) accounts for 90% to 95% of HL cases. The remaining 5% to 10% of cases have historically been classified as nodular lymphocyte–predominant HL; although this terminology was retained in the fifth edition of the World Health Organization classification, the latest International Consensus Classification has retermed nodular lymphocyte–predominant HL as nodular lymphocyte–predominant B-cell lymphoma, reflecting pathologic and clinical differences between the 2 entities.[2,3] Treatment of cHL includes novel agents, such as brentuximab vedotin, a CD30-targeted antibody-drug conjugate, and anti–programmed cell death 1 (PD-1) immunotherapy as part of regimens for some patients with unfavorable early-stage cHL, all patients with advanced-stage cHL, and those with relapsed or refractory cHL. Because cure is achieved in approximately 90% of patients, de-escalation of therapy has become a focus of study to minimize treatment-related morbidity among the typically young patients with a diagnosis of cHL.

This Review summarizes current evidence regarding the pathogenesis, epidemiology, diagnosis, and management of cHL in adults aged 18 years and older.

Methods

We performed a PubMed search for English-language articles related to cHL published from January 1, 2010, to April 23, 2026, using the following major Medical Subject Headings and title keywords: ("*Hodgkin Disease*"[Majr] OR *hodgkin**[ti]), excluding case reports, letters, editorials, and animal studies. This search retrieved 5145 articles. We also reviewed guidelines from the National Comprehensive Cancer Network (NCCN)[4] and European Society for Medical Oncology.[5] Additional articles, including publications before 2010, were identified from references. This Review includes 125 articles, composed of 69 observational studies, 37 clinical trials, 9 narrative reviews, 4 systematic reviews or meta-analyses, and 6 guideline recommendations.

Discussion

Pathogenesis

The malignant cell in cHL is the Reed-Sternberg cell, which is derived from germinal-center B lymphocytes. Unlike normal germinal-center B lymphocytes, Reed-Sternberg cells do not express certain surface proteins, such as the B-cell receptor.[6,7] To avoid apoptosis, Reed-Sternberg cells rely on dysregulated signaling, including through the nuclear factor–κB,[8-10] Janus kinase–signal transducer and activator of transcription (JAK-STAT),[11-13] and phosphoinositide 3-kinase–protein kinase B (PI3K-AKT) pathways.[14]

Reed-Sternberg cells, which represent less than 2% of cHL tumor volume, are typically surrounded by an extensive inflammatory infiltrate, produced by chemokines that cause an influx of immune cells into the tumor microenvironment (**Figure 1**).[15] Strategies by which Reed-Sternberg cells evade immune surveillance include near-uniform copy number variations (a genomic phenomenon in which sections of DNA are repeated) of chromosome 9p24.1 and the associated PD-1 ligand (PD-L1) loci, leading to increased expression of PD-L1.[16,17] Reed-Sternberg cells with PD-L1 overexpression bind to PD-1 receptors on surrounding tumor-infiltrating immune effectors (such as T cells), triggering an inhibitory cascade that suppresses T-cell function and allows tumor cells to avoid destruction.

Epidemiology and Risk Factors

In the United States, there were an estimated 8720 incident cases of HL in 2025 and 1150 deaths due to HL, accounting for 10% of all lymphoma diagnoses and 0.4% of all cancers.[18] Classic HL has a bimodal age distribution, with an initial peak at age 15 to 35 years and a second, smaller peak at approximately age 70 years.[19] The median age at diagnosis is 33 years; only 18% of cases are diagnosed in individuals older than 65 years.[20,21]

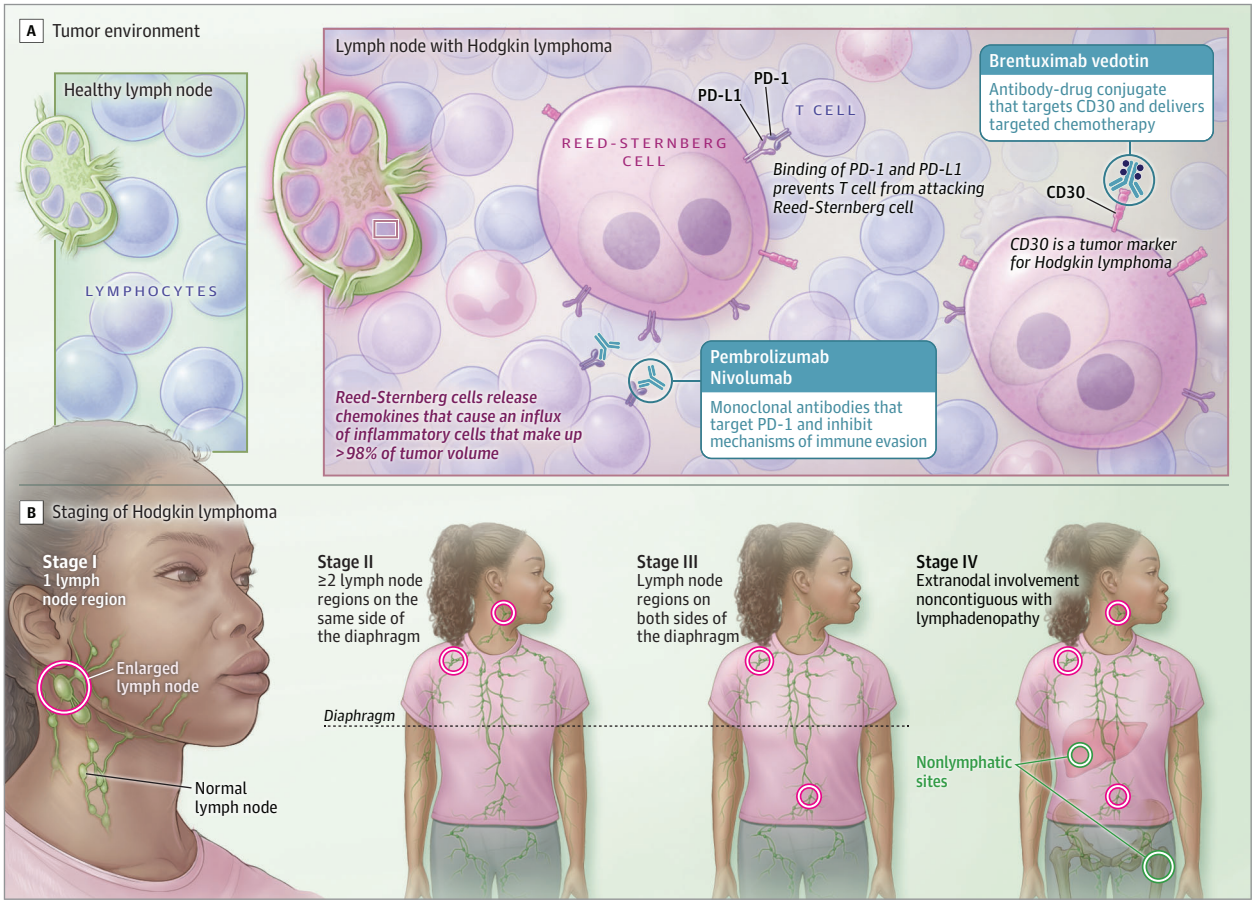
Although specific causes remain unknown, several risk factors have been associated with cHL development (**Box 1**). First, studies have demonstrated a familial predisposition for cHL. A pedigree analysis of 36 families with 2 or more first-degree relatives with HL identified 44 recurrent gene variants that may predispose to HL,[22] and high-risk polymorphisms in major histocompatibility complex loci have been identified.[23-25] An observational study that followed up 366 sets of twins for a mean of 14 years reported an increased risk of HL in monozygotic twins of patients with HL: 10 of 179 sets of monozygotic twins became concordant for HL compared with 0 of 187 sets of dizygotic twins (standardized incidence ratio [SIR], 99; 95% CI, 48-182).[26] Similarly, in a large European cohort study of 57 475 first-degree relatives of 13 922 patients with HL, first-degree relatives had a 0.6% cumulative risk of HL, for an SIR of 3.3 (95% CI, 2.8-3.9).[27]

Epstein-Barr virus (EBV) infection has also been associated with cHL. A cohort study of 38 555 Danish and Swedish patients reported that the risk of EBV-positive cHL was significantly increased (relative risk, 4.0; 95% CI, 3.4-4.5) after infection with EBV, with a median incubation time of 4.1 years (95% CI, 1.8-8.3 years).[28] However, the absolute risk of developing cHL after EBV infection is low, estimated at approximately 0.1% in this cohort.[29] Rates of EBV positivity differ among histologic subtypes of cHL and by geographic region, with comparatively higher rates of EBV-positive cHL in Africa, Central America, and South America compared with the United States and Europe.[30,31]

The incidence of cHL is also increased in patients with immune-mediated disorders, including those with personal[32,33] or family histories[33] of sarcoidosis, systemic lupus erythematosus, and Sjögren disease. In a study of 878 161 Swedish patients with a diagnosis of 33 immune-mediated diseases between 1964 and 2010, 371 incident cases of HL were diagnosed, reflecting an SIR of 2.0 (95% CI, 1.8-2.2).[32] The risk of cHL—particularly EBV-positive disease—is also increased among immunosuppressed patients. A meta-analysis assessing the incidence of cHL among patients with immunodeficiency, which included 7 cohort studies of people with HIV/AIDS (n = 444 172) and 4 cohort studies of transplant recipients (n = 29 087), demonstrated an increased risk of cHL in both populations. Among the 7 studies of people with HIV/AIDS, 802 cases of HL were observed (0.18%; SIR, 11.03; 95% CI, 8.43-14.4).[34] Among the 4 studies of transplant recipients (n = 29 087), 21 cases of HL were observed (0.07%; SIR, 3.89; 95% CI, 2.42-6.26).[34]

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Figure 1. Illustration of Tumor Environment and Clinical Staging of Classic Hodgkin Lymphoma



A, The malignant cell in classic Hodgkin lymphoma is the Reed-Sternberg cell (RSC). RSCs are typically surrounded by an extensive inflammatory infiltrate composed of macrophages, T cells, neutrophils, eosinophils, and mast cells.

B, Classic Hodgkin lymphoma is staged using the Lugano classification, which is derived from Ann Arbor staging. PD-1 indicates programmed cell death 1; and PD-L1, PD-1 ligand.

Additionally, certain immunosuppressive medications have been associated with increased risk of cHL.[35] In a cohort study of 189 289 patients with inflammatory bowel disease who were followed up for a median of 6.7 years, HL incidence was increased among patients treated with thiopurines (azathioprine and 6-mercaptopurine), anti–tumor necrosis factor agents (infliximab and adalimumab), or both (25 of 50 405, 0.05%) compared with those not treated with these medications (30 of 123 069, 0.024%).[35] In this study, the hazard ratio (HR) of developing cHL was 2.83 (95% CI, 1.37-5.84) after use of thiopurines alone, 2.23 (95% CI, 0.81-6.13) after use of anti–tumor necrosis factor agents alone, and 12.1 (95% CI, 4.46-33.1) after combination therapy.[35]

Subtypes

The 2022 World Health Organization classification outlined 4 histologic subtypes of cHL, reflecting the microscopic appearance of the cHL tumor: nodular sclerosis, mixed cellularity, lymphocyte rich, and lymphocyte depleted.[2] In the United States, approximately 75% of cases are nodular sclerosis subtype, 20% are mixed cellularity, 5% are lymphocyte rich, and less than 1% are lymphocyte depleted.[36] In regions other than North America and Europe, the prevalence of mixed-cellularity and lymphocyte-depleted cases—subtypes associated with EBV positivity—is higher.[36,37] Furthermore, the mixed-cellularity subtype is more prevalent in older patients (≥60 years),[38] and the mixed-cellularity and lymphocyte-depleted subtypes are more common among patients with immunodeficiency.[39]

Recently, attempts have been made to define distinct clusters of cHL based on genomic profiling of circulating tumor DNA (ctDNA).[40-42] However, these molecular subtypes have not been incorporated into consensus guidelines because of heterogeneity in classification schemes and lack of universal access to ctDNA sequencing platforms.

Clinical Presentation

Most patients with cHL present with painless supradiaphragmatic lymphadenopathy involving cervical, mediastinal, supraclavicular, and axillary lymph nodes, detected by patients or clinicians on physical examination.[43] However, some patients—particularly those with asymptomatic mediastinal involvement—may have lymphadenopathy detected incidentally on imaging performed for evaluation of other conditions (**Figure 2**). Isolated infradiaphragmatic lymphadenopathy occurs in less than 10% of patients.[44] Classic HL typically spreads from the index lymph node to adjacent lymph nodes via lymphatic channels.[45] Noncontiguous spread, hematogenous dissemination, or

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both are uncommon but more frequently occur in immunosuppressed patients.[46]

B (systemic/constitutional) symptoms, including fevers (>38.3 °C), drenching sweats, and unintentional weight loss (>10% of body weight during the preceding 6 months), are present in 30% to 40% of patients.[47] Pruritus, which occurs in approximately 10% to 15% of patients and can precede the diagnosis of cHL by months, is typically generalized and not associated with a rash. The pruritus can result in severe excoriations and is often resistant to topical therapies.[48] Less than 10% of patients report severe pain at lymphatic or bony sites involved by cHL after ingestion of alcohol; this phenomenon of alcohol-associated pain is highly specific for cHL, but the mechanism has not been elucidated.[49]

Diagnosis

The diagnosis of cHL is made on detection of Reed-Sternberg cells in a polymorphous inflammatory infiltrate in a biopsy specimen. Excisional lymph node biopsies are preferred over core needle biopsies because of the scarcity of Reed-Sternberg cells in the tumor specimen and the importance of tissue architecture to identify histologic subtypes.[4,50] On immunohistochemistry, the Reed-Sternberg cells typically express CD30 and CD15, have weak expression of PAX5, and lack classic B-cell antigens (CD19, CD20, and CD79a) and the common leukocyte antigen (CD45).[2]

Staging

Classic HL is staged anatomically using Lugano classification,[51] which was derived from Ann Arbor staging (Figure 1).[52] Staging is performed with ^{18}F-fludeoxyglucose–positron emission tomography/computed tomography (FDG-PET/CT) scans, which have improved accuracy compared with CT.[53] Stage I involves a single lymphatic site (eg, nodal region, thymus, spleen, the tonsillar ring) or a single nonlymphatic organ or site (eg, bone, lung, liver) in the absence of nodal involvement (stage IE [for extranodal]). Stage II involves 2 or more nodal regions on the same side of the diaphragm or a single nonlymphatic organ or site with regional lymph node involvement (IIE). Stage III involves nodal regions on both sides of the diaphragm, and stage IV reflects diffuse involvement of nonlymphatic organs. The staging in cHL also includes presence (B) or absence (A) of B symptoms. Routine bone marrow evaluation is generally not required for staging because patients with early-stage disease have a low incidence of bone marrow involvement, and FDG-PET/CT is highly sensitive for bone involvement.[54] In an analysis of 10 912 patients with HL included in the Surveillance, Epidemiology, and End Results database, the stage at diagnosis was 15% stage I, 41% stage II, 23% stage III, and 21% stage IV.[55] Retrospective series have reported that older patients (≥60 years) more frequently present with advanced-stage disease (stage III or IV), with estimates ranging from 60% to 70% at diagnosis.[56]

Risk Stratification

Multiple risk-stratification systems have been developed for cHL to assist with prognostication and treatment selection. Early-stage cHL (stage I or II) is classified into favorable or unfavorable disease, reflecting the presence of high-risk features. Three risk-stratification systems (NCCN, European Organisation for Research and Treatment of Cancer, and German Hodgkin Study Group), which include risk factors such as age, B symptoms, disease bulk, number of nodal sites, presence of extranodal disease, and high erythrocyte sedimentation rate, perform similarly in discriminating high-risk patients (**Table 1**).[4,57] The definition of disease bulk used in the NCCN, European Organisation for Research and Treatment of Cancer, and German Hodgkin Study Group risk-stratification systems is greater than 10 cm for a nodal mass or greater than one-third of the internal transverse diameter of the thorax at T5 to T6 for a mediastinal mass, measured on chest radiograph.[52] In a retrospective analysis of 185 patients with cHL treated between 2000 and 2010, the optimal definition of bulk predictive of inferior outcomes was a maximum tumor diameter of greater than 7 cm on CT.[58]

Box 1. Frequently Asked Questions About Classic Hodgkin Lymphoma

What are risk factors for classic Hodgkin lymphoma (cHL)?
Multiple factors have been associated with an increased risk of developing cHL, including Epstein-Barr virus infection; personal or family history of immune-mediated disorders, such as sarcoidosis, systemic lupus erythematosus, and Sjögren disease; long-standing immunosuppression; and familial predisposition.

What is the treatment and prognosis for cHL?
Early-stage cHL (stage I or II) is treated with chemotherapy with or without consolidative radiotherapy, whereas advanced-stage cHL (stage III or IV) is treated with chemotherapy alone. Novel agents, including brentuximab vedotin and anti–programmed cell death 1 immunotherapy, have been incorporated into regimens for early-stage unfavorable and advanced-stage disease. Patients with relapsed or refractory cHL who meet eligibility criteria should undergo high-dose chemotherapy and autologous stem cell transplant, with curative intent. The overall prognosis of cHL is excellent, with cure in approximately 90% of patients.

What are potential treatment-related complications among cHL survivors?
Survivors of cHL are at risk for secondary malignancies (most commonly non-Hodgkin lymphoma and breast, lung, and colorectal cancer), cardiovascular dysfunction (including coronary disease, cardiomyopathy, and valvular dysfunction), pulmonary toxicity (including pulmonary fibrosis, obstructive pulmonary disease, and recurrent pneumonia), and hypothyroidism, especially among patients who received radiation, intensive chemotherapy, or both.

Treatment

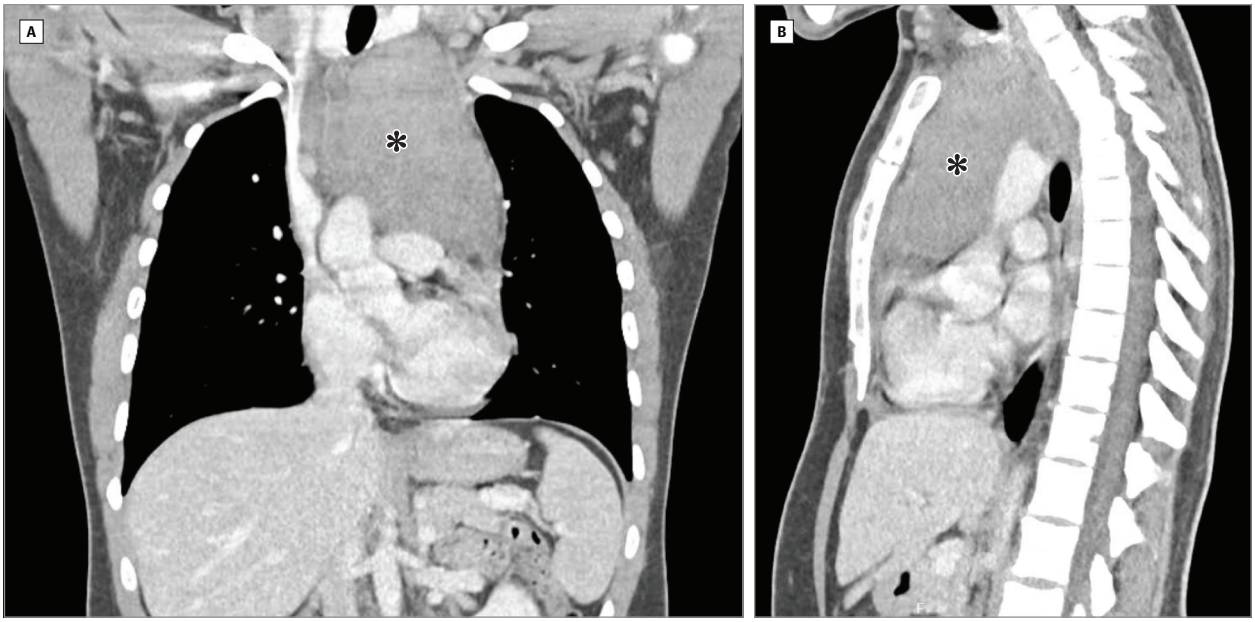
Early-Stage Disease

The current guideline-recommended treatment for patients with early-stage cHL (stage I or II) is chemotherapy with or without consolidative radiotherapy (RT) (**Figure 3**).[4,5]

Patients with early-stage cHL treated with chemotherapy and RT typically have superior progression-free survival (PFS) than those receiving chemotherapy alone. However, overall survival (OS) is similar with both approaches because of the efficacy of salvage regimens for relapsed or refractory disease.[59-61] Therefore, the decision to include RT depends on patient factors, such as age, comorbidities, location of disease, and the risk of secondary malignancies or long-term cardiopulmonary dysfunction (eg, coronary disease, valvular dysfunction, pulmonary fibrosis). Guidelines also recommend incorporation of an interim FDG-PET/CT scan (usually obtained after 2 cycles of treatment) because presence of a complete

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Figure 2. Computed Tomographic Scans Demonstrating Mediastinal Involvement by Classic Hodgkin Lymphoma



Asterisk indicates a bulky anterior mediastinal mass on coronal (A) and sagittal (B) views, causing mediastinal widening.

Table 1. Unfavorable Risk Factors in Early-Stage Hodgkin Lymphoma[a]

Risk factor	NCCN	EORTC	GHSG
Age, y		≥50	
ESR, mm/h, and B symptoms	≥50 or any B symptoms	≥50 if no B symptoms; ≥30 if B symptoms	≥50 if no B symptoms; ≥30 if B symptoms
Mediastinal mass	MMR >0.33	MTR >0.35	MMR >0.33
No. of nodal sites	>3	>3	>2
Extranodal lesion			Any
Bulky	>10 cm		

Abbreviations: EORTC, European Organisation for Research and Treatment of Cancer; ESR, erythrocyte sedimentation rate; GHSG, German Hodgkin Study Group; MMR, mediastinal mass ratio (maximum width of mass/maximum intrathoracic diameter, as measured on chest radiograph); MTR, mediastinal thoracic ratio (maximum width of mediastinal mass/intrathoracic diameter at T5-T6, as measured on chest radiograph); NCCN, National Comprehensive Cancer Network.

[a] The 3 risk-stratification systems were developed by different groups (NCCN, EORTC, and GHSG) and vary slightly in their included criteria. All 3 perform similarly in discriminating high-risk patients. In practice, which classification system is used depends on geography and clinician preference; no one risk-stratification system is clearly superior.

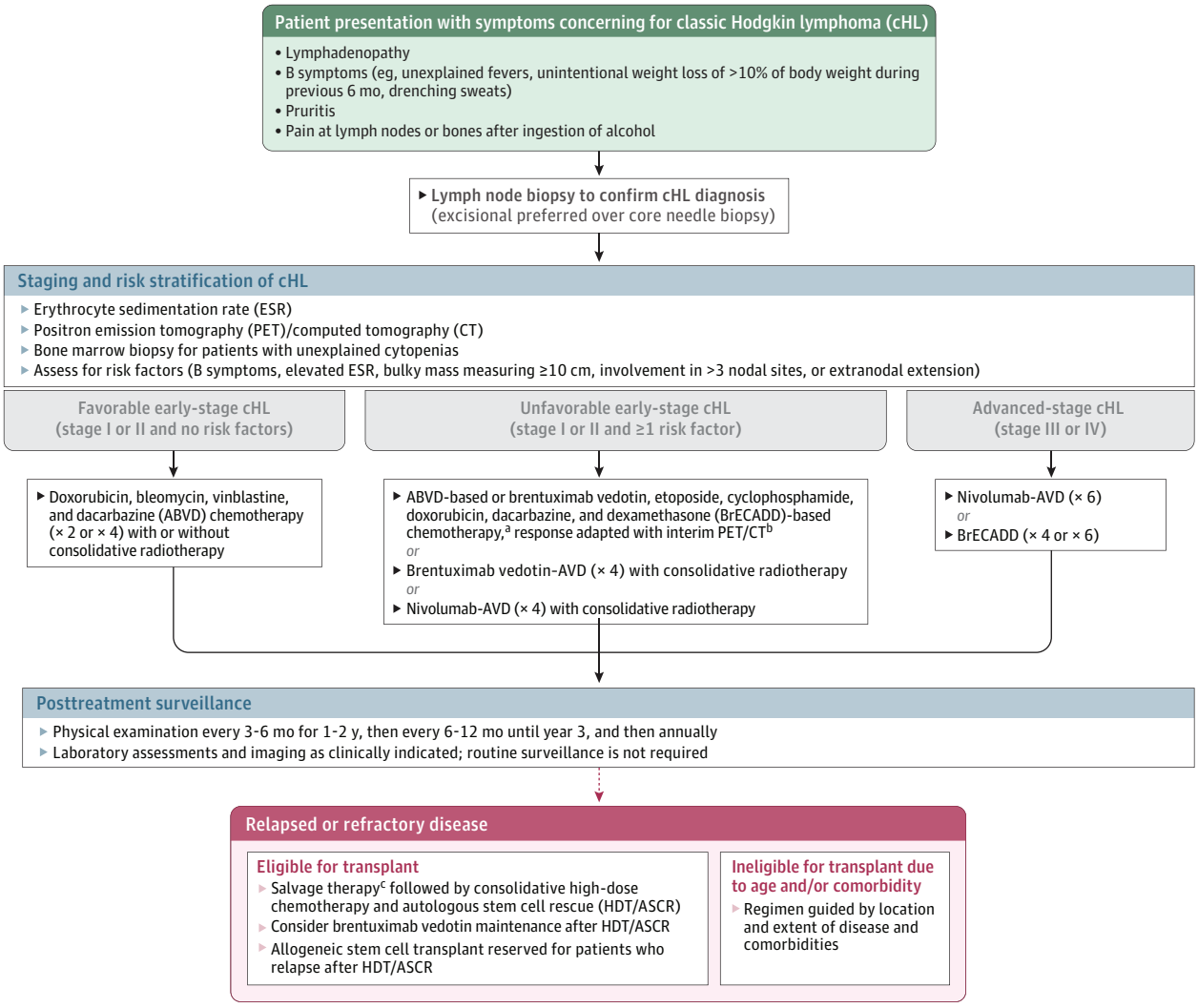
response, defined as absence of residual metabolically active tumor, on interim FDG-PET/CT is favorably prognostic and allows for the de-escalation of treatment.[62]

Patients with favorable early-stage cHL (0 risk factors) are treated with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy with or without consolidative RT (**Table 2**).[59-61,63,64] The initial phase 3 trial establishing ABVD and 20-Gy RT as a standard approach in patients with early-stage favorable disease randomized 1370 patients with early-stage favorable cHL to 4 groups: ABVD (× 4) and 30-Gy RT, ABVD (× 4) and 20-Gy RT, ABVD (× 2) and 30-Gy RT, and ABVD (× 2) and 20-Gy RT.[63] At 5-year follow-up, there was no significant difference in freedom-from-treatment failure between the highest-intensity group (ABVD [× 4] and 30-Gy RT) and the lowest-intensity group (ABVD [× 2] and 20-Gy RT) (92.8% vs 91.2%; absolute difference, −1.6%; 95% CI, −6.3% to 3.1%), meeting the noninferiority threshold of 7%.[63]

More recent trials involving favorable early-stage cHL have investigated omission of RT, using response-adapted approaches with interim PET/CT.[59-61,64] These studies have demonstrated that inclusion of RT improves PFS but does not affect OS. For instance, a phase 3 trial randomized 754 patients with favorable early-stage cHL to ABVD (× 3) and 30-Gy RT or ABVD (× 2) followed by a PET-guided approach, in which patients with PET-negative results received 2 additional cycles of ABVD without RT.[60,61] Among patients with PET-negative results, 10-year PFS was improved with RT (98.8% for ABVD [× 3] and 30-Gy RT vs 85.4% for ABVD [× 4] alone; HR, 13.2; 95% CI, 3.1-55.8). However, OS at 10-year follow-up was unchanged, at 100% and 98%, respectively (HR, 2.80; 95% CI, 0.29-26.9).[61] Similarly, in a phase 3 trial that enrolled 602 patients with stage IA or IIA cHL without bulk, all patients received ABVD (× 3) followed by an interim PET-guided approach, which involved randomizing patients with PET-negative results to RT (30 Gy) or no

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Figure 3. Illustration of Overview of the Diagnosis and Management of Classic Hodgkin Lymphoma



AVD indicates ABVD without bleomycin.

[a]BrECADD can be used for patients with stage IIB disease and either a large mediastinal mass or extranodal lesions.

[b]A PET scan is obtained midtreatment and determines the number of subsequent cycles, use of radiation, and/or change in treatment.

[c]Salvage therapy is referring to second-line treatment with combination chemotherapy ± immunotherapy. There are several options from which the treating physician can choose.

further treatment.[59] Among patients with PET-negative results, 3-year PFS (per protocol) was 97.1% for those randomized to RT vs 90.8% for those who received no further therapy (rate ratio, 2.36; 95% CI, 1.13-4.95). However, 3-year OS was unchanged, at 97.1% vs 99.0%, respectively (rate ratio, 0.51; 95% CI, 0.15-1.68). Because omission of RT does not affect OS, an RT-free approach is considered in select patients for whom the reduction in long-term risk of secondary malignancies or organ dysfunction outweighs the slightly higher risk of cHL relapse. Although this decision is individualized, RT is more likely to be omitted for younger patients and for those with cHL located close to organs that could be negatively affected by radiation exposure (ie, breast, lung, or heart).

In accordance with consensus guidelines, patients with unfavorable early-stage disease (≥1 risk factor) can be treated with either chemotherapy-only regimens or combined-modality therapy incorporating both novel agents and RT (Table 2).[65-69] A phase 3 trial investigating chemotherapy-only regimens enrolled patients with stage IIA cHL with adverse features (bulk or ≥3 involved nodal regions), stage IIB disease, or stage III-IV disease.[65] Patients received ABVD (× 2) followed by a PET-guided approach, in which patients with PET-negative results were randomized to 4 additional cycles of ABVD vs 4 additional cycles of AVD (with bleomycin omitted). Among patients with stage II disease (42% of the cohort), 7-year PFS was 84.7% (95% CI, 81.0%-87.7%) and 7-year OS was 95.6% (95% CI, 93.2%-97.2%).[66] Among all patients with PET-negative results (n = 933), 7-year PFS was 81% for ABVD vs 79.2% for AVD (HR, 1.10; 95% CI, 0.82-1.47), supporting omission of bleomycin for patients who had PET-negative results after 2 cycles of chemotherapy.[66] Another phase 3 trial explored the integration of brentuximab vedotin, a CD30-targeted antibody-drug conjugate,

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Table 2. Summary of Selected Trials for Early-Stage Classic Hodgkin Lymphoma

Trial[a]	Phase	Eligibility criteria	Study regimen	Control group	Patients (No.)	PFS and OS (study vs control, if randomized)	Common grade ≥3 adverse events in study group (>5%)
Early-stage favorable							
GHSG HD10, 2010[63]	3	Stage I or II without risk factors (by GHSG criteria)	Multiple study groups (A, B, C, and D): ABVD (× 4) + 20-Gy RT (A) ABVD (× 2) + 30-Gy RT (B) ABVD (× 2) + 20-Gy RT (C)	ABVD (× 4) + 30-Gy RT (D)	1370	5-y PFS: 93.2% (A) vs 90.8% (B) vs 91.6% (C) vs 93.9% (D) 5-y OS: 97.3% (A) vs 96.6% (B) vs 96.6% (C) vs 96.9% (D)	Alopecia (15.2%-28.1%, depending on study group), leukopenia (14.9%-23.5%), nausea/vomiting (8.7%-13.4%), infection (1.7%-5.1%)
EORTC/LYSA/FIL H10F, 2014[60,61]	3	Stage I or II without risk factors (by EORTC criteria)	ABVD (x 4) only (for iPET2-negative patients)	ABVD (× 3) + RT	357 (iPET2 negative)	10-y PFS: 85.4% vs 98.8% 10-y OS: 98.0% vs 100.0%	Graded AEs not reported
RAPID, 2015[59]	3	Stage IA or IIA without disease bulk	ABVD (× 3) only (for iPET3-negative patients)	ABVD (× 3) + RT (for iPET3-negative patients)	420 (iPET3 negative)	3-y PFS: 90.8% vs 94.6% (intention to treat)/97.1% (per protocol) 3-y OS: 99.0% vs 97.1%	Graded AEs not reported
CALGB 50604, 2018[64]	2	Stage I or II without disease bulk	ABVD (× 2) followed by PET-guided approach: iPET2 negative: ABVD (× 2) iPET2 positive: escBEACOPP (× 2) + RT	NA	149	3-y PFS, iPET negative: 91% 3-y PFS, iPET positive: 66%	Neutropenia (70%), leukopenia (37%), febrile neutropenia (6%), lymphopenia (6%)
Early-stage unfavorable, without bulk							
CALGB 50604, 2018[64]	2	Stage I or II without disease bulk	ABVD (× 2) followed by PET-guided approach: iPET2 negative: ABVD (× 2) iPET2 positive: escBEACOPP (× 2) + RT	NA	149	3-y PFS, iPET negative: 91% 3-y PFS, iPET positive: 66%	Neutropenia (70%), leukopenia (37%), febrile neutropenia (6%), lymphopenia (6%)
Early-stage unfavorable, with bulk							
Chemotherapy only							
RATHL, 2016[65,66]	3	Stage IIA with bulk or ≥3 areas of lymph node involvement; stage IIB-IV	ABVD (× 2) followed by AVD (× 4) (for iPET2-negative patients)	ABVD (× 6)	933 (iPET2 negative)	7-y PFS: 79.2% vs 81% 7-y OS: 93.5% vs 93.2%	Neutropenia (58%), infection and/or febrile neutropenia (7%)
GHSG HD21, 2024[67]	3	Stage IIB with bulk or extranodal lesions; stage III-IV	BrECADD (× 4-6, PET guided)	escBEACOPP (× 4-6, PET guided)	1500	4-y PFS: 94.3% vs 90.9% 4-y OS: 98.6% vs 98.2%	Leukopenia (87%), thrombocytopenia (55%), anemia (30%), febrile neutropenia (28%), infection (20%), gastrointestinal disorders (8%), hepatobiliary disorders (5%)
Chemotherapy and RT							
BREACH, 2023[68]	2	Stage I or II with risk factors (by EORTC criteria)	Brentuximab vedotin-AVD (× 4) + RT	ABVD (× 4) + RT	170	2-y PFS: 97.3% vs 92.6%	Neutropenia (75%), leukopenia (35%), gastrointestinal disorders (12%), infections (8%), febrile neutropenia (8%), AST/ALT increase (6%)
NIVAHL, 2023[69]	2	Stage IA-IIA with risk factors (by GHSG criteria); stage IIB with either elevated ESR or ≥3 areas of lymph node involvement	Nivolumab-AVD (× 4) + RT	Nivolumab (× 4) + nivolumab-AVD (× 2) + AVD (× 2) + RT	109	3-y PFS: 100% vs 98% 3-y OS: 100% vs 100%	None >5%

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AVD, ABVD without bleomycin; BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone; EORTC, European Organisation for Research and Treatment of Cancer; escBEACOPP, escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; ESR, erythrocyte sedimentation rate; FIL, Italian Lymphoma Foundation; GHSG, German Hodgkin Study Group; iPET, interim positron emission tomography/computed tomography; LYSA, Lymphoma Study Association; NA, not applicable; OS, overall survival; PFS, progression-free survival; RT, radiotherapy.

[a] Trials were selected based on their clinical relevance and effect on current management.

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into first-line therapy. This study randomized 1500 patients with advanced-stage cHL (defined as stage IIB with either large mediastinal mass or extranodal lesions or as stage III-IV) to BrECADD (× 4-6) (a combination of brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone) or escalated BEACOPP (× 4-6) (a combination of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone). In this trial, among the patients with stage II disease (16% of the cohort), use of BrECADD was associated with improved PFS compared with escalated BEACOPP, with 4-year PFS of 96.5% (95% CI, 93.2%-99.9%) vs 90.3% (95% CI, 85.0%-95.9%), respectively.[67]

Combined-modality therapy using novel agents such as brentuximab vedotin or anti–PD-1 immunotherapy (nivolumab) followed by RT has also been studied in early-stage unfavorable disease. A phase 2 trial randomized 170 patients with early-stage unfavorable cHL to brentuximab vedotin–AVD (× 4) or ABVD (× 4), both followed by RT (30 Gy). Two-year PFS was higher with brentuximab vedotin–AVD (97.3%; 95% CI, 91.9%-99.1%) compared with ABVD (92.6%; 95% CI, 81.4%-97.2%).[68] Another phase 2 study randomized 109 patients with early-stage unfavorable cHL to concomitant therapy with nivolumab-AVD (× 4) and RT (30 Gy) or sequential therapy with nivolumab (× 4) followed by nivolumab-AVD (× 2), AVD (× 2), and RT (30 Gy).[69] In this trial, 3-year PFS was 100% and 98% (95% CI, 95%-100%) in the concomitant and sequential groups, respectively.[69] Based on these studies, both brentuximab vedotin–AVD and concurrent nivolumab-AVD followed by RT are included in guidelines for early-stage unfavorable cHL.[4] In practice, the decision to use a combined-modality regimen instead of a chemotherapy-only regimen is similarly based on the potential long-term morbidity associated with RT.

Advanced-Stage Disease

Current guideline-recommended treatment for patients with advanced-stage cHL (stage III-IV) is chemotherapy combined with novel agents (**Table 3**).[4,67,70-81] The preferred regimen in the United States is nivolumab-AVD, based on a phase 3 trial that randomized 970 patients with advanced-stage cHL to nivolumab-AVD (× 6) or brentuximab vedotin–AVD (× 6).[70,71] Three-year PFS was 91% with nivolumab-AVD compared with 82% for brentuximab vedotin–AVD (HR, 0.48; 95% CI, 0.34-0.69), and OS was 98% and 97%, respectively (HR, 0.48; 95% CI, 0.20-1.15).[70,71]

For patients ineligible for immunotherapy because of autoimmune disease or comorbidities requiring active immunosuppression, guideline-recommended treatment options include brentuximab vedotin–containing regimens, such as BrECADD or brentuximab vedotin–AVD.[67,72,73] BrECADD was assessed in the aforementioned phase 3 trial.[67] In the subset of patients who had stage III-IV disease (84% of the cohort), 4-year PFS was 93.9% (95% CI, 91.9%-95.9%) in the BrECADD group compared with 91.0% (95% CI, 88.7%-93.4%) in the brentuximab vedotin–AVD group.[67] In another phase 3 trial that randomized 1334 patients with stage III-IV disease to brentuximab vedotin–AVD (× 6) or ABVD (× 6), brentuximab vedotin–AVD led to improved 6-year PFS (82.3% vs 74.5%; HR, 0.68; 95% CI, 0.53-0.86) and 6-year OS (93.9% vs 89.4%; HR, 0.59; 95% CI, 0.40-0.88).[72] For older adults (≥60 years) who are eligible for combination chemotherapy, both nivolumab-AVD and sequential brentuximab vedotin–AVD (in which patients receive brentuximab vedotin [× 2] followed by AVD [× 6] and brentuximab vedotin [× 4]) have been well tolerated.[82,83]

Relapsed or Refractory Disease

Patients with suspected relapsed cHL (recurrence after initial remission) or refractory disease (nonresponse to primary treatment) should undergo a biopsy to confirm the ongoing presence of cHL. Approximately 10% to 15% of patients experience relapsed or refractory disease, with most relapses occurring in the first 2 years after completion of first-line therapy.[84] Guideline-recommended care for relapsed or refractory cHL is salvage chemotherapy followed by consolidative high-dose chemotherapy and autologous stem cell transplant (Table 3).[4] Salvage chemotherapy typically consists of 2 to 4 cycles of treatment given during 6 to 12 weeks, closely followed by myeloablative high-dose chemotherapy administered throughout several days during the week preceding autologous stem cell rescue. Eligibility for stem cell transplant is determined based on performance status; comorbidities; organ dysfunction; psychosocial factors, such as caregiver availability and treatment adherence; and, when applicable, geriatric assessment to assess eligibility in older adults.

Although multiple salvage regimens have been studied in cHL, including pembrolizumab with gemcitabine, vinorelbine, and liposomal doxorubicin[74,75]; brentuximab vedotin with ifosfamide, carboplatin, and etoposide (ICE)[76,77]; nivolumab-ICE[80]; pembrolizumab-ICE[79]; and brentuximab vedotin–nivolumab,[78] to date they have not been compared in randomized trials. However, a retrospective study of 1280 patients with relapsed or refractory cHL treated between 2010 and 2022 reported that those who received immunotherapy before autologous stem cell transplant had higher 2-year PFS compared with those who received brentuximab vedotin–based or chemotherapy-only salvage regimens (88.2%, 70.2%, and 67.4%, respectively; $P < .001$).[85] Because this study included patients who were treated before inclusion of anti–PD-1 immunotherapy in first-line therapy, the optimal choice of salvage regimen is uncertain.

After autologous stem cell transplant, guidelines recommend consideration of maintenance therapy with brentuximab vedotin for high-risk patients who have not previously received this medication.[4,5] This recommendation is based on a phase 3 trial that randomized 329 patients not previously treated with brentuximab vedotin and with high-risk relapsed or refractory cHL (defined as refractory disease, relapse with an initial remission duration of <12 months, or extranodal involvement at relapse) to brentuximab vedotin (× 16) or placebo, starting 30 to 45 days after autologous stem cell transplant. In this trial, 5-year PFS was 59% with brentuximab vedotin vs 41% with placebo (HR, 0.52; 95% CI, 0.38-0.72).[81]

Allogeneic stem cell transplant is generally reserved for eligible patients who experience cHL relapse after autologous stem cell transplant. In a retrospective analysis of 2186 patients who received allogeneic stem cell transplant for relapsed or refractory cHL, 12-month PFS was 61% (95% CI, 58%-63%) and OS was 78% (95% CI, 76%-80%).[86] However, nonrelapse-related mortality is estimated at 15% within 1 year of allogeneic stem cell transplant, so patients must be carefully selected for this procedure.[86]

For patients ineligible for autologous stem cell transplant, treatment should be individualized according to the location and extent of disease and comorbidities and is generally considered palliative

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Table 3. Summary of Selected Trials for Advanced-Stage and Relapsed or Refractory Classic Hodgkin Lymphoma

Trial[a]	Phase	Eligibility criteria	Study regimen	Control group	Patients, No.	PFS and OS (study vs control, if randomized)	Common grade ≥3 adverse events in study group (>5%)
Advanced stage							
Anti-PD-1 immunotherapy							
SWOG 1826, 2024[70,71]	3	Stage III-IV	Nivolumab-AVD (× 6)	Brentuximab vedotin-AVD (× 6)	970	3-y PFS: 91% vs 82% 3-y OS: 98% vs 97%	Neutropenia (48%), leukopenia (15%), anemia (6%), lymphopenia (6%), febrile neutropenia (6%), ALT increased (5%)
Brentuximab vedotin							
ECHELON-1, 2022[72,73]	3	Stage III-IV	Brentuximab vedotin-AVD (× 6)	ABVD (× 6)	1334	6-y PFS: 82.3% vs 74.5% 6-y OS: 93.9% vs 89.4%	Neutropenia (54%), neuropathy (5%)
GHSG HD21, 2024[67]	3	Stage IIB with bulk or extranodal lesions; stage III-IV	BrECADD (× 4-6, PET guided)	escBEACOPP (× 4-6, PET guided)	1500	4-y PFS: 94.3% vs 90.9% 4-y OS: 98.6% vs 98.2%	Leukopenia (87%), thrombocytopenia (55%), anemia (30%), febrile neutropenia (28%), infection (20%), gastrointestinal disorders (8%), hepatobiliary disorders (5%)
Relapsed or refractory							
Salvage chemotherapy and HDT/ASCR							
Pembrolizumab-GVD + HDT/ASCR, 2021[74,75]	2	Primary refractory or first relapse	Pembrolizumab-GVD (× 2-4) + HDT/ASCR	NA	39	5-y PFS: 91% 5-y OS: 94%	Neutropenia (10%), AST/ALT increased (10%), mucositis (5%)
Brentuximab vedotin-ICE + HDT/ASCR, 2021[76,77]	1, 2	Primary refractory or first relapse	Brentuximab vedotin-ICE (× 2-3) + HDT/ASCR	NA	45	5-y PFS: 77% 5-y OS: 91%	Thrombocytopenia (80%), neutropenia (73%), anemia (13%), sepsis (13%), ALT increase (11%), hypophosphatemia (11%), febrile neutropenia (9%), hypokalemia (9%), hyperglycemia (7%)
Brentuximab vedotin-nivolumab + HDT/ASCR, 2021[78]	1, 2	Primary refractory or first relapse	Brentuximab vedotin-nivolumab (× 4) + HDT/ASCR	NA	93	3-y PFS: 77% 3-y OS: 93%	Neutropenia (5%)
Pembrolizumab-ICE + HDT/ASCR, 2023[79]	2	Relapsed or refractory after 1-2 lines of therapy	Pembrolizumab-ICE (× 2-3) + HDT/ASCR	NA	42	2-y PFS: 87.2% 2-y OS: 95.1%	Thrombocytopenia (76%), anemia (48%), leukopenia (40%), neutropenia (36%), hypokalemia (10%), hypertension (10%), hypophosphatemia (7%), AST/ALT increased (5%)
Nivolumab-ICE + HDT/ASCR, 2025[80]	2	Primary refractory or first relapse, with high-risk features	Nivolumab (× 1) + nivolumab-ICE (× 2-3) + HDT/ASCR	NA	35	2-y PFS: 88% 2-y OS: 100%	Lymphopenia (20%), leukopenia (17%), neutropenia (14%), anemia (11%), thrombocytopenia (9%)
Maintenance after HDT/ASCR							
AETHERA, 2018[81]	3	Post-HDT/ASCR with high-risk features	Brentuximab vedotin (× 16)	Placebo	329	5-y PFS: 59% vs 41%	Neutropenia (29%), peripheral sensory neuropathy (10%), peripheral motor neuropathy (6%)

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AVD, ABVD without bleomycin; BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone; escBEACOPP, escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; GHSG, German Hodgkin Study Group; GVD, gemcitabine, vinorelbine, liposomal doxorubicin; HDT/ASCR, high-dose chemotherapy and autologous stem cell rescue; ICE, ifosfamide, cyclophosphamide, etoposide; NA, not applicable; OS, overall survival; PD-1, programmed cell death 1; PET, positron emission tomography; PFS, progression-free survival.

[a] Trials were selected based on their clinical relevance and effect on current management.

instead of curative. Guideline-recommended options include brentuximab vedotin–nivolumab,[78] anti–PD-1 immunotherapy in combination with single-agent chemotherapy[87] or epigenetic modifiers such as the histone deacetylase inhibitor vorinostat,[88] brentuximab vedotin in combination with single-agent chemotherapy,[89,90] or chemotherapy alone.[91]

Treatment strategies that potentially omit high-dose chemotherapy and autologous stem cell transplant for relapsed or refractory

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cHL are being investigated in clinical trials. A phase 2 study treated patients who had achieved complete response after salvage pembrolizumab with gemcitabine, vinorelbine, and liposomal doxorubicin (× 4) with 1 year of pembrolizumab maintenance.[92] Two-year PFS was 51% (95% CI, 33%-80%); however, 9 of 10 patients who relapsed underwent autologous stem cell transplant in the third-line setting and achieved complete response.[92] Another phase 2 study treated children, adolescents, and young adults (up to 30 years) with low-risk relapsed cHL (n = 28) with brentuximab vedotin–nivolumab (× 4), followed by brentuximab vedotin–nivolumab (× 2) or brentuximab vedotin–bendamustine (× 2) based on interim PET/CT, and RT. Three-year PFS and OS were 95.0% (90% CI, 76.7%-99.0%) and 100%, respectively.[93] These study data suggest that select patients with relapsed or refractory cHL may be cured without high-dose chemotherapy and autologous stem cell rescue.

Prognosis

Based on clinical trials with at least 2 years of follow-up, estimated OS is greater than 97% for early-stage favorable disease,[60,61,63] greater than 95% for early-stage unfavorable disease,[65-69] and greater than 90% for advanced-stage disease,[67,70-72] with PFS greater than 85% to 90%, depending on the chosen regimen. For patients with relapsed or refractory disease, across multiple studies PFS is greater than 75% to 80% and OS is greater than 90% after autologous stem cell transplant.[75,77-80] Individuals who undergo allogeneic stem cell transplant have an estimated PFS of 40% to 60% and OS of 60% to 70%.[86] In real-world analyses (retrospective studies of patients treated outside of clinical trials), the 5-year relative survival rate for cHL is 88%, with most cHL-related mortality occurring in older patients with advanced-stage disease.[94,95]

Survivorship

According to NCCN guidelines, surveillance after curative treatment for cHL includes physical examination every 3 to 6 months for 1 to 2 years, then every 6 to 12 months until year 3, and then annually (**Box 2**). Blood testing and imaging should be obtained only as clinically indicated due to the limited utility of surveillance blood testing in detecting relapse and lack of demonstrated survival benefit with routine surveillance imaging.[4,96,97]

Survivors of cHL are at risk for treatment-related complications. Secondary malignancies are the leading cause of death in cHL survivors.[98] In a study of 3905 patients in the Netherlands who had survived at least 5 years after initiation of treatment for HL, 1055 second cancers were diagnosed in 908 patients, for an SIR of 4.6 (95% CI, 4.3-4.9).[99] The most common second malignancies were non-Hodgkin lymphomas or solid tumors, including breast, lung, and colorectal cancer.[99] The risk of myelodysplasia is also increased among survivors of cHL compared with the general population (SIR, 9.5; 95% CI, 6.8-12.9). However, the risk of secondary acute myeloid leukemia has decreased because highly leukemogenic agents are no longer included in first-line therapy.[99,100] Survivors of cHL are also at increased risk of skin cancers (melanoma and nonmelanoma subtypes) and thyroid cancer, particularly if they received RT.[101-103] The timing of diagnosis of secondary cancers varies by histology, with myelodysplasia risk peaking 5 to 9 years after chemotherapy and solid tumors typically developing greater than 10 years posttreatment.[104,105] The risk of secondary malignancies can remain elevated for more than 25 years, especially among patients receiving RT.[99,104,105] For women who received RT to the mediastinum or axilla between ages 10 and 30 years, the NCCN recommends annual breast screening (both mammography and magnetic resonance imaging) starting at age 25 years.[4]

Cardiovascular disease is the leading cause of non–cancer-related death among cHL survivors.[106] Increased cardiovascular risk (coronary disease, cardiomyopathy, conduction abnormalities, valvular disorders, and pericardial disease) emerges 5 to 10 years after treatment and remains elevated throughout life.[98,106] In a cohort study of 2524 HL survivors with a median follow-up of 20 years, 1713 cardiovascular events were identified in 797 patients, with SIRs of 3.2 (95% CI, 3.0-3.5) for coronary disease and 6.8 (95% CI, 5.9-7.6) for heart failure.[107]

Classic HL survivors also have an increased risk of pulmonary fibrosis, obstructive pulmonary disease (asthma and chronic obstructive pulmonary disease), chronic pleural effusions, and recurrent pneumonia, particularly among patients treated with bleomycin or RT or those with a history of smoking.[108,109] A Danish cohort study of 1474 patients with cHL demonstrated a 10-year cumulative risk of pulmonary disease of 7.4% compared with 2.9% for age-matched comparators (HR, 2.91; 95% CI, 2.30-3.68), with a 10-year cumulative risk of 4.1% for interstitial lung disease (HR, 15.84;

Box 2. Follow-Up Recommendations

Follow-up after completion of treatment (up to 5 years):
- History and physical examination every 3 to 6 months for 1 to 2 years, then every 6 to 12 months until year 3, and then annually
- Complete blood cell count (CBC) and chemistry panel as clinically indicated; erythrocyte sedimentation rate if elevated at diagnosis
- Thyroid function tests at least annually if thyroid gland was in the radiation field
- Echocardiogram at 1 year after completion of anthracycline therapy
- Imaging only if there is clinical concern for relapse
- Annual influenza vaccine and other vaccines as clinically indicated

Follow-up and monitoring after 5 years:
- Consider transfer to primary care physician, referral to survivorship clinic, or both
- History and physical examination every year
- CBC count and chemistry panel every year
- Thyroid function tests at least annually if thyroid gland was in the radiation field
- Biannual lipid screening
- Annual fasting glucose level
- Consider echocardiogram every 5 to 10 years
- Consider carotid ultrasonography every 10 years if neck was in the radiation field
- Annual breast screening (mammography and magnetic resonance imaging) for women aged 25 years or older who received radiation to the mediastinum or axilla between ages 10 and 30 years
- Routine screening for other cancers (cervical, colorectal, lung, and prostate cancer) as appropriate according to NCCN and American Cancer Society screening guidelines
- Annual influenza vaccine and other vaccines as clinically indicated

Adapted from the National Comprehensive Cancer Network (NCCN).[4]

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95% CI, 9.35-26.84) and 3.5% for chronic obstructive pulmonary disease (HR, 1.99; 95% CI, 1.43-2.76) among patients with cHL.[110] Patients who received RT to the neck also have an increased risk of thyroid dysfunction, most commonly hypothyroidism, with an incidence of 30% to 50%, depending on the dose of RT, and also have an increased risk of Graves disease and benign thyroid nodules.[101]

Because many patients receive a diagnosis of cHL at a young age, fertility preservation (including sperm banking or oocyte cryopreservation) should be discussed before treatment initiation. Patients who receive treatment with alkylating agents (particularly escalated BEACOPP), pelvic irradiation, or autologous stem cell transplant are at increased risk for fertility complications, such as premature ovarian failure and azospermia.[111]

Future Directions

Several studies have demonstrated that ctDNA sequencing can detect minimal residual disease in cHL.[40-42,112,113] Secondary analyses of several cHL clinical trials have shown that persistence of detectable ctDNA is negatively prognostic and may be more sensitive than conventional FDG-PET/CT assessment in predicting disease relapse.[114-116] An ongoing phase 2 trial is using ctDNA to guide treatment de-escalation for patients with advanced-stage disease.[117] Furthermore, novel investigational therapies, including but not limited to chimeric antigen receptor T-cell therapy, are being evaluated in clinical trials.[118-124] Chimeric antigen receptor T-cell therapy has provided durable remissions for some patients with relapsed or refractory non-Hodgkin lymphoma but is not approved or commercially available for patients with relapsed or refractory cHL.[125]

Limitations

This review has several limitations. First, some relevant studies may have been missed. Second, a systematic evaluation of the quality of evidence was not performed. Third, this review did not discuss management of children and young adolescents (<18 years) with cHL because there are important differences in the care of these patients, including different risk-stratification systems and chemotherapy regimens.

Conclusions

First-line treatment for cHL is chemotherapy, with addition of RT for some patients with early-stage disease. Select patients with unfavorable early-stage cHL and all patients with advanced-stage cHL should also receive anti–PD-1 immunotherapy or a CD30-targeted antibody-drug conjugate in addition to chemotherapy. Patients with relapsed or refractory cHL should be evaluated for stem cell transplant. With treatment, cure is achieved in up to 90% of patients with both early-stage and advanced-stage disease.

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