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Hodgkin Lymphoma

A mini review for clinicians

For postgraduate residents (medical, radiation and paediatric oncology, haematology, pathology, nuclear medicine, general surgery, medicine), practising clinicians and medical students

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CONTENTS

01 At a glance

02 Clinical presentation, common traps & causes

03 Diagnosis, workup & staging essentials

04 Biology and biomarkers that change treatment

05 Local therapy: radiotherapy & surgery

06 Systemic therapy: indications & options

07 Management algorithms

08 Survivorship, follow-up & late effects

09 Landmark trials

10 Practice pearls & pitfalls

11 Case vignettes: lines of management

12 References & guidelines

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Updated 16 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Hodgkin Lymphoma

Haematological cancers, part 1 · Classic Hodgkin lymphoma in adults · PET-adapted ABVD, N-AVD and BrECADD · Relapse and transplant · NLPHL · Children, adolescents and pregnancy · Survivorship · Key points for clinicians · Last updated 16 October 2026

01 At a glance

- **Hodgkin lymphoma (HL) is two diseases.** Classic HL (cHL, about 95%) has rare malignant Hodgkin/Reed-Sternberg (HRS) cells inside a large crowd of inflammatory cells; nodular lymphocyte-predominant HL (NLPHL, about 5%) is an indolent B-cell lymphoma with its own treatment.
- **It is one of the most curable cancers:** 5-year survival is above 95% in early favourable disease, above 90% in early unfavourable disease and 85–90% in advanced disease with modern treatment.
- **The Indian picture differs:** in the OncoCollect registry (939 patients, 9 centres) the median age was 38, men outnumbered women about 2:1, mixed cellularity made up 61% of cases and five-year overall survival was 84% ([Bhurani 2022](#)^[1]). In tropical and resource-limited regions nearly all cHL is EBV-positive.
- **Treatment follows three things:** stage (Lugano, by PET-CT), risk group (early favourable, early unfavourable, advanced) and the PET response after two cycles. The aim is to cure with the least treatment that keeps relapse rare.
- **First-line options have changed:** nivolumab plus AVD (N-AVD) is now preferred for advanced disease ([S1826](#)^[2]); BrECADD suits fit adults up to 60 ([HD21](#)^[3]); early-stage disease is still treated with PET-adapted ABVD, with or without low-dose radiotherapy.
- **Relapse is not the end:** checkpoint-inhibitor-based salvage followed by an autologous transplant cures more than half of relapsed patients.
- **Survivors need lifelong care:** second cancers and heart disease cause most late deaths; radiotherapy fields, anthracycline dose and bleomycin decide each person's screening plan.
- **India trap:** many patients first receive anti-tuberculosis treatment without a biopsy (16% of adults at Tata Memorial, [Jain 2015](#)^[4]; 29% of children in a 396-child study, [Mahajan 2023](#)^[5]), which delays diagnosis.

Two diseases share the name: classic Hodgkin lymphoma and NLPHL

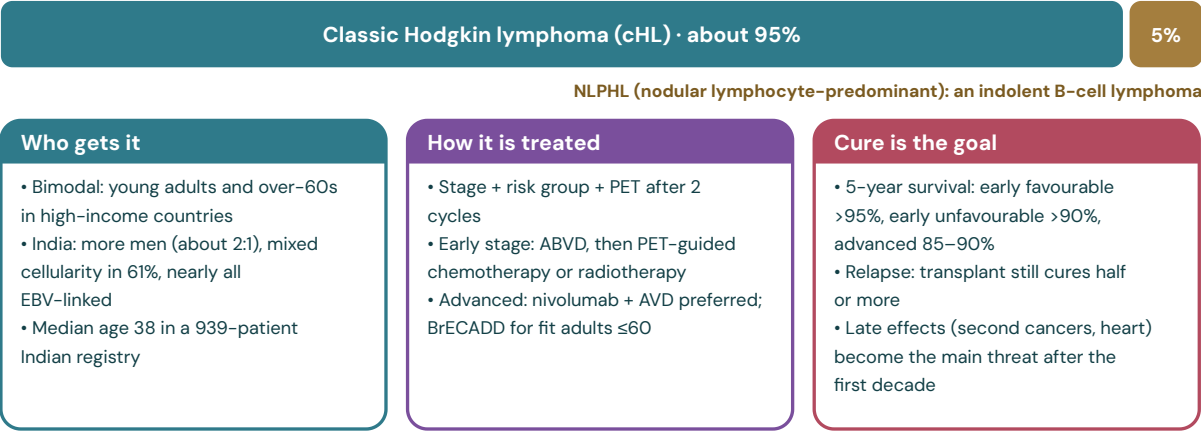
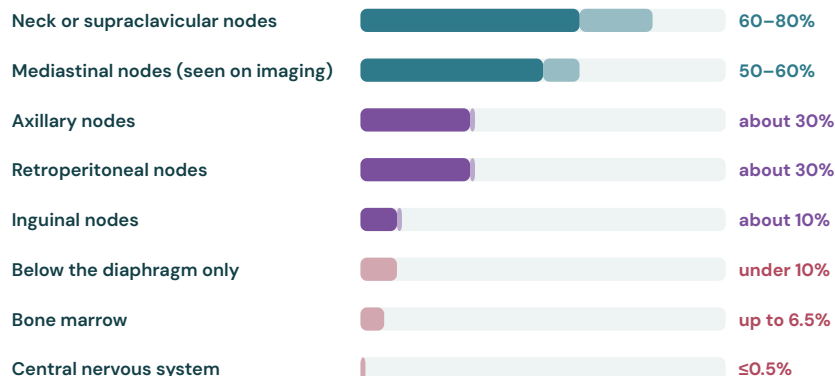


Figure 1. Hodgkin lymphoma at a glance. Survival figures from the UpToDate survivorship review; Indian profile from the OncoCollect registry (9 centres, 2011–2017). NLPHL is treated like an indolent B-cell lymphoma, not like classic Hodgkin lymphoma.

02 Clinical presentation, common traps & causes

Where classic Hodgkin lymphoma shows up at diagnosis



Nodes are painless, firm and rubbery. Spread is usually contiguous, from one node group to the next; skipped regions suggest immunosuppression (HIV).

Symptoms

- B symptoms in about 40%: under 20% in stage I–II, up to half in advanced
- Itch in 10–15%, sometimes months before the nodes
- Pain minutes after alcohol: under 10%, but very specific

Blood clues

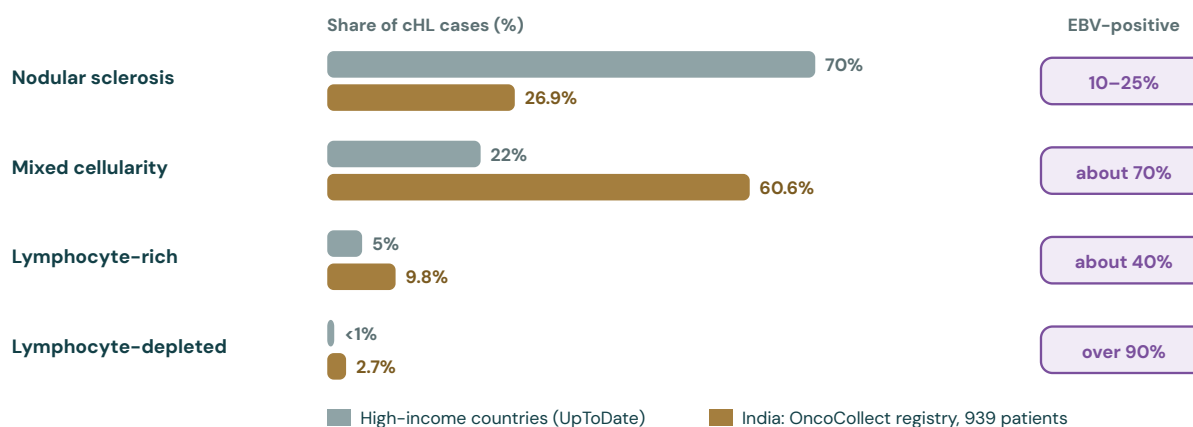
- Microcytic anaemia that looks like iron deficiency
- Eosinophilia, high ESR, low albumin
- High calcium (calcitriol), nephrotic syndrome: rare

Figure 2. Presentation. Percentages from the UpToDate cHL presentation review; lighter bars show a reported range. Mediastinal disease is usually silent and found on a chest film or CT.

Who gets it, and why

- **Age:** in high-income countries most cases are 15–35 years old, with a second peak in older adults; in resource-limited settings there is a childhood peak in boys and a prominent peak in older adults. HL is the commonest cancer of adolescents.
- **EBV:** EBV is found in about 70% of mixed cellularity, more than 90% of lymphocyte-depleted, about 40% of lymphocyte-rich and 10–25% of nodular sclerosis cHL; almost always in HIV-associated cases. After infectious mononucleosis the absolute risk of cHL is only about 1 in 1000.
- **Immunity:** people living with HIV have a 5- to 25-fold higher risk; transplant recipients and people on immunosuppressants for autoimmune disease are also at higher risk. cHL is not an AIDS-defining cancer.
- **Family:** first-degree relatives have a 3- to 5-fold higher risk (siblings more than parents; identical twins far higher); HLA region variants contribute. HL is not contagious.

Histological subtypes: the Indian pattern differs from the Western one



The subtype rarely changes adult treatment, but mixed cellularity and EBV point to the age, sex and stage pattern seen in Indian clinics.

Figure 3. Subtypes and EBV. Western shares and EBV rates from the UpToDate cHL review; Indian shares from the OncoCollect registry (Bhurani 2022). In tropical and resource-limited regions nearly all cHL is EBV-positive.

Common traps

- **Anti-TB treatment without a biopsy.** A neck node with fever and weight loss is treated as TB for months; patients then arrive with advanced disease, low albumin and poorer fitness. Biopsy a persistent node before starting anti-TB drugs. Note that about 15% of cHL nodes contain granulomas: a granuloma on a small sample does not exclude lymphoma.
- **FNAC reported as "reactive" or "suspicious".** Fine-needle aspiration cannot make or exclude the diagnosis. Ask for an excision (or several cores).
- **Biopsying the wrong node.** Neck, supraclavicular and axillary nodes are preferred; inguinal nodes are often distorted by old inflammation.
- **Mediastinal mass biopsied by a thin needle.** CT-guided or endobronchial samples are often too small or crushed; mediastinoscopy, an anterior mediastinotomy or VATS gives a diagnosis.
- **Itch treated as a skin disease** for months; it can precede nodes. **Microcytic anaemia treated as iron deficiency** when it is cytokine-driven.
- **Pain after alcohol** is rare but very specific for cHL. **Fever that waxes and wanes** over 1–2 weeks (Pel-Ebstein) is rare.
- **Mimics:** anaplastic large cell lymphoma, primary mediastinal B-cell lymphoma, mediastinal grey-zone lymphoma, T-cell/histiocyte-rich large B-cell lymphoma, and EBV-positive mucocutaneous ulcer can all imitate cHL; an expert haematopathologist settles most of them.

SHARE WITH PATIENTS: SWELLINGS, SYMPTOMS AND WHO GETS LYMPHOMA

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Every swollen lymph node is cancer?

A painless neck swelling is always tuberculosis?

If there is no pain, fever or weight loss, lymphoma is impossible?

A normal blood count rules out lymphoma?

Lymphoma occurs only in elderly people?

Lymphoma is contagious and can spread between family members?

03 Diagnosis, workup & staging essentials

Making the diagnosis

- **Tissue:** excisional or incisional node biopsy is preferred; several core biopsies may suffice; FNAC is not adequate for diagnosis or subtyping.
- **Pathology:** HRS cells (classic, mononuclear Hodgkin, lacunar or mummified variants) in a mixed inflammatory background; HRS cells express CD30 (virtually all) and usually CD15 (75–85%), and lack CD45 and CD3; B-cell markers are absent or weak, PAX5 is weakly positive, BOB1 and OCT2 are reduced. EBV is shown by EBER in situ hybridisation.
- **Subtype:** nodular sclerosis, mixed cellularity, lymphocyte-rich, lymphocyte-depleted. In adults the subtype does not change treatment.

Reading the immunostains: classic HL, NLPHL and the lymphomas that imitate them

	Classic HL (HRS cells)	NLPHL (LP or "popcorn" cells)
CD30	+ (virtually all)	– (rarely +)
CD15	+ in 75–85%	–
CD45	–	+
CD20 and B-cell program	absent or weak in a subset	+ (strong)
PAX5	weak +	+
BOB1, OCT2	reduced or lost	+
EBV (EBER)	variable; most cases in India	rare
Background	mixed inflammatory cells, fibrosis	small B cells, CD57+ T-cell rosettes

ALCL • CD30 strong, CD15 –, PAX5 – • T-cell antigens +, ALK ±, cytotoxic +	PMBL • Pan-B +, CD30 weak, CD15 rare • Primary mediastinal B-cell lymphoma	THRLBCL • B-cell +; CD15, CD30, EBV – • T-cell/histiocyte-rich LBCL	Grey-zone lymphoma • CD15 + strong CD30 + B markers • Worse outlook than cHL, PMBL
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Figure 4. Immunostains. A diagnosis rests on morphology plus phenotype in an excised node; ask for an expert haematopathologist when the pattern is unusual. Marker patterns from the UpToDate cHL and NLPHL diagnosis reviews.

Before treatment

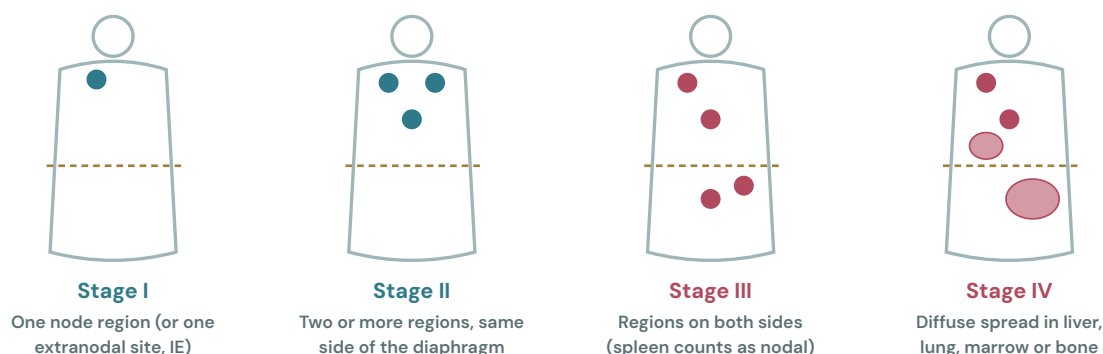
Area	What to do	Why
History and examination	B symptoms, itch, alcohol pain; every node region, liver and spleen; performance status; smoking; heart and lung disease; prior cancers and family history	Stage, risk group, fitness, late-effect risk
Blood tests	CBC with differential, ESR, electrolytes, kidney and liver tests, calcium, albumin, LDH	ESR sets the early-stage risk group; IPS factors
Viruses	HBsAg and anti-HBc (HBV DNA if positive), HCV antibody and RNA, HIV	Antiviral prophylaxis; HIV care
Heart	Echocardiogram or MUGA: LVEF ≥50% for doxorubicin	Baseline for anthracycline; STOP-CA^[6] : atorvastatin slowed EF decline, no proven fall in heart failure

Area	What to do	Why
Lungs	Pulmonary function tests with DLCO: $\geq 60\%$ for bleomycin	Bleomycin lung injury
Imaging	PET-CT skull base to mid-thigh; diagnostic contrast CT where anatomy matters (neck CT before neck RT); chest X-ray for a mediastinal mass	Lugano stage; bulk; baseline for PET2. If PET is unavailable, contrast CT chest-abdomen-pelvis
Bone marrow	Only for unexplained cytopenias with a marrow-negative PET	PET finds marrow disease
Fertility and pregnancy	Pregnancy test; counselling; sperm banking; ovarian options if intensive treatment is likely	ABVD rarely causes infertility; BEACOPP-type treatment and transplant do
Other	Stop smoking; vaccines (no live vaccines once on treatment); psychosocial support	Lung, heart and second-cancer risk

Staging and risk groups

- Lugano staging ([Cheson 2014](#)^[7]): stage I–II = early (limited), III–IV = advanced; add A or B, the size of any bulky mass (≥ 10 cm, or a mediastinal mass over one-third of the thoracic diameter) and E for limited contiguous extranodal extension.
- Early-stage disease is favourable or unfavourable by EORTC, GHSG or NCCN criteria (Figure 6). Use the criteria of the trial whose regimen you follow, especially for the abbreviated GHSG approach.
- Advanced disease is scored with the International Prognostic Score ([Hasenclever 1998](#)^[8]; ABVD-era outcomes, [Moccia 2012](#)^[9]) or the A-HIPI calculator ([Rodday 2023](#)^[10]).
- EBV positivity carries a worse prognosis in adults aged 45 and over; it is not yet used to choose treatment.

Lugano staging in four pictures (the dashed line is the diaphragm)



A or B: B = fever over 38°C, drenching night sweats, or loss of more than 10% of weight in 6 months (itch and fatigue are not B symptoms). Bulk: a mass of 10 cm or more, or a mediastinal mass over one-third of the thoracic diameter. E: limited extension into a neighbouring organ from a nodal site (stage I–II only). Staging is by PET-CT; bone marrow biopsy only for unexplained cytopenias.

Figure 5. Lugano staging (derived from Ann Arbor with the Cotswolds modifications). Stage I–II = early (limited) disease; stage III–IV = advanced.

From stage to treatment group

Early favourable

- Stage I–II with none of the risk factors of the chosen group
- GHSG favourable (strictest): ≤ 2 regions, no E, ESR < 50 (or < 30 with B), mediastinum $< 1/3$
- Only GHSG–favourable patients qualify for the shortest course (2 ABVD + 20 Gy)

Early unfavourable

- EORTC: age > 50 , mediastinum $> 1/3$, high ESR*, ≥ 4 sites
- GHSG: mediastinum $> 1/3$, high ESR*, ≥ 3 sites, extranodal disease
- NCCN adds any mass > 10 cm
- *ESR ≥ 50 , or ≥ 30 with B symptoms

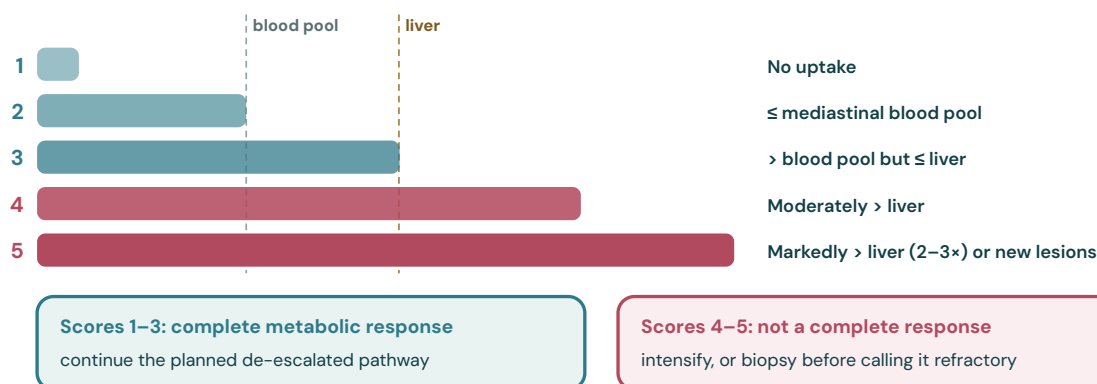
Advanced

- Stage III–IV (some trials include IIB with bulk or E)
- International Prognostic Score, 1 point each: albumin < 4 g/dL, Hb < 10.5 g/dL, male, age > 45 , stage IV, WBC $\geq 15,000$, lymphocytes < 600 or $< 8\%$
- A–HIPI calculator also available

IPS and 5-year freedom from progression with ABVD: 0 factors 88% · 1: 84% · 2: 80% · 3: 74% · 4: 67% · 5 or more: 62% (Moccia 2012).

Figure 6. Treatment groups. Use the prognostic system of the trial whose regimen you follow; the three systems label about 55% of early-stage patients as unfavourable (UpToDate staging review).

Reading interim and end-of-treatment PET: the five-point (Deauville) scale



X = new uptake unlikely to be lymphoma (infection, inflammation, thymic rebound, sarcoid-like reaction to immunotherapy).

Time the end-of-treatment PET 6–8 weeks after chemotherapy or 3 months after radiotherapy, once inflammation has settled.

Figure 7. Deauville scale. It compares the hottest residual site with the patient's own blood pool and liver, so scans from different machines can be read the same way (Lugano 2014).

SHARE WITH PATIENTS: SCANS AND STAGING

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[A lymph node that lights up on PET always means cancer?](#)

[Stage IV lymphoma means the disease is incurable?](#)

[FNAC alone can reliably diagnose every lymphoma?](#)

[All lymphomas are the same cancer?](#)

o4 Biology and biomarkers that change treatment

Why two antibody drugs work so well: the HRS cell and its crowd

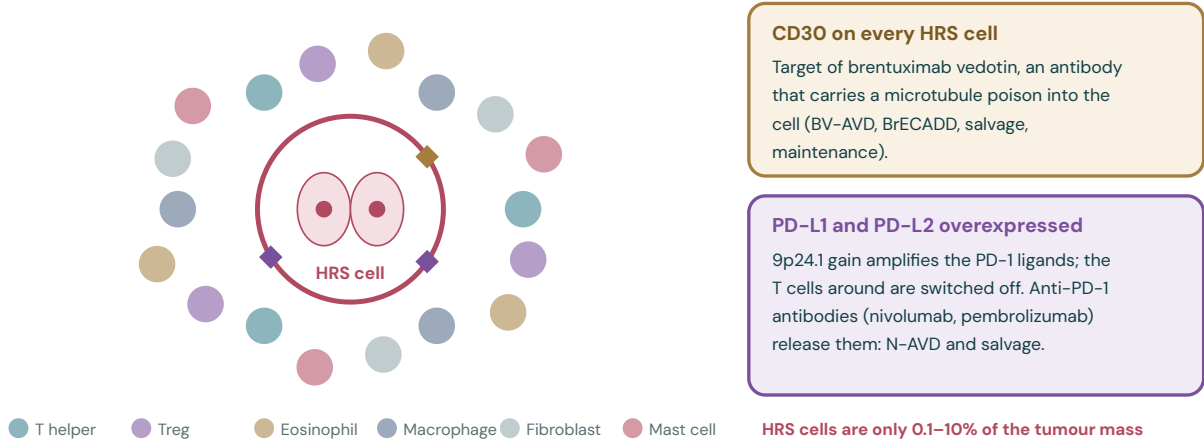


Figure 8. Biology that drives treatment. HRS cells evade the immune crowd around them; CD30 and the PD-1 pathway are the two targets that changed first-line and relapse therapy (UpToDate cHL pathogenesis review).

Marker or feature	What it tells you	What it changes
Interim PET (Deauville score after 2 cycles)	Chemosensitivity in this patient	The single most important guide: de-escalation (drop bleomycin, omit RT, 20 Gy in GHSG favourable) or escalation (more cycles, BrECADD, biopsy)
CD30 on HRS cells	Present in virtually every cHL	Target for brentuximab vedotin (BV-AVD, BrECADD, salvage, maintenance)
9p24.1 gain: PD-L1 and PD-L2 overexpression	Immune escape; nearly universal in cHL	Explains the high activity of nivolumab and pembrolizumab (N-AVD, salvage)
EBV (EBER)	Most cases in India; nearly all in HIV	Prognostic in older adults; suggests checking HIV; not a treatment selector
ESR, albumin, Hb, WBC, lymphocyte count	Inflammatory burden	Early-stage risk group (ESR); IPS for advanced disease
CD20 on the malignant cells	NLPHL (LP cells) rather than cHL	Rituximab-based treatment, RT or watching; not ABVD
Histological subtype of cHL	Epidemiology and EBV link	Does not change adult treatment
Circulating tumour DNA subtypes	Inflammatory, virally driven or oncogene-driven groups	Investigational

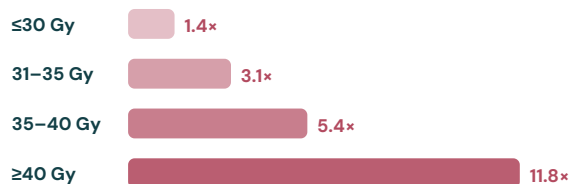
05 Local therapy: radiotherapy & surgery

Radiotherapy

- **Involved-site RT (ISRT)** treats the originally involved sites with a margin, at 20–30 Gy; the old mantle and extended fields (35–44 Gy) explain most of the heart disease and breast cancer seen in survivors treated before 2000.
- **20 Gy** after two ABVD cycles is reserved for patients who meet every GHSG favourable criterion and have a PET2 Deauville score of 1–3 ([HD16^{\[11\]}](#)): 5-year PFS 93% with RT vs 86% without; overall survival 98% in both).
- **30 Gy** is used after chemotherapy in combined modality therapy (CMT), after four cycles for slow responders (PET4 Deauville 1–4), and for a single PET-positive residual site.
- **Adding RT after a negative PET2 prevents relapses but does not improve survival** ([H10^{\[12\]}](#), [RAPID^{\[13\]}](#), [HD16^{\[11\]}](#)): the choice weighs age, sex, sites (breast, heart, lung) and the patient's preference, ideally with both a medical and a radiation oncologist.
- **Advanced disease:** no consolidation RT for bulky disease in complete metabolic response ([H0607^{\[14\]}](#): no PFS difference whether the mass was 5–7, 8–10 or over 10 cm).
- **Technique:** IMRT or VMAT, deep-inspiration breath-hold and contouring of heart substructures lower the dose to the heart; protons help selected mediastinal cases.
- **Other roles:** palliation in frail patients; consolidation of bulky or unirradiated sites around autologous transplant; NLPHL stage IA (30–36 Gy).

Radiotherapy: excellent local control, but heart and breast remember the dose

Relative risk of valve disease by dose to the valve (Dutch cohort)



Coronary disease rises in a straight line with mean heart dose: about 2.5-fold at 20 Gy. Risk lasts 25 years or more and adds to anthracycline risk.

Modern involved-site RT, IMRT/VMAT and breath-hold lower the heart dose.

Lean towards chemotherapy only

- Young woman whose breasts would be in the field
- 2–3 thoracic sites, poor lung function, heavy smoking
- Strong heart risk factors or family history of early heart disease

Lean towards adding radiotherapy

- Disease away from heart, lungs and breasts (for example neck only)
- Wish to shorten chemotherapy or limit anthracycline
- Slow interim PET response (Deauville 4–5 after 2 cycles)

Figure 9. Weighing radiotherapy. Old mantle fields used 35–44 Gy; today's 20–30 Gy involved-site fields carry far less risk, but not none (Cutter 2015; van Nimwegen 2016; UpToDate cardiotoxicity and early-stage reviews).

Surgery

- Surgery is for diagnosis: an excision biopsy, or a mediastinoscopy, anterior mediastinotomy or VATS for a mediastinal mass. There is no role for debulking in cHL.
- In NLPHL, a completely excised stage IA node may be watched (with more relapses than after RT); see section 06.
- Before anaesthesia for a large mediastinal mass, plan with the anaesthetist: airway or SVC compression can worsen under general anaesthesia.

o6 Systemic therapy: indications & options

Early favourable disease (stage I–II, no risk factors)

- **Start with ABVD × 2, then PET2:** ABVD is given on days 1 and 15 of 28-day cycles without delays or dose cuts for neutropenia and without routine G-CSF. Newer combinations have not been tested against PET-adapted ABVD in early-stage disease.
- **PET2 Deauville 1–3 and all GHSG favourable criteria:** 20 Gy ISRT and stop ([HD16](#)^[11]).
- **PET2 1–3, other favourable criteria:** either chemotherapy only (ABVD × 2 more if ≤60 with healthy lungs; AVD × 2 more if over 60 or with lung disease; up to 4 more cycles for Deauville 3 or larger volume, checking PFTs before more bleomycin) or CMT (ABVD × 1 more, then 30 Gy). In [H10F](#)^[12], CMT gave 10-year PFS 98.8% vs 85.4% for chemotherapy alone, with overall survival 100% vs 98%. [CALGB 50604](#)^[15] supports chemotherapy alone after a negative PET2.
- **Single site of Deauville 4:** ABVD × 2 more, then PET4: 1–3 → 30 Gy; 4–5 → biopsy (no lymphoma → 30 Gy; lymphoma → refractory pathway).
- **Multiple Deauville 4 sites or any Deauville 5:** biopsy first.
- **No PET available:** CMT with ABVD × 3 and 30 Gy ISRT (GHSG favourable: ABVD × 2 and 20 Gy) rather than chemotherapy alone, because relapses cannot be predicted.

Early unfavourable disease (stage I–II with risk factors)

- **ABVD × 2, then PET2.**
- **PET2 Deauville 1–3:** either CMT (ABVD × 2 more, then 30 Gy) or chemotherapy only with AVD × 4 (bleomycin dropped). In [H10U](#)^[12], 10-year overall survival was 94.8% vs 94.3% and PFS 86.5% vs 91.4% (chemotherapy only vs CMT), with 20 of 22 relapses in the chemotherapy arm at previously involved sites. [RATHL](#)^[16] showed AVD equal to ABVD after a negative PET2 with less lung toxicity. Even bulky disease did well without RT after a negative PET2 ([CALGB 50801](#)^[17]: ABVD × 6, 3-year PFS 93%).
- **PET2 Deauville 4–5:** ABVD × 2 more or BrECADD × 2 (with G-CSF), then PET4: 1–4 → 30 Gy; 5 → biopsy.
- **Alternatives** used by some experts when CMT is planned: N-AVD × 4 + 30 Gy ([NIVAH](#)^[18]: 3-year PFS 99%); BV-AVD × 4 + 30 Gy ([BREACH](#)^[19]: more PET2 negativity but no PFS gain and more toxicity); BrECADD for stage IIB with a large mediastinal mass or extranodal disease ([HD21](#)^[3]).

Advanced disease (stage III–IV)

First-line choices for advanced classic HL (no doses: follow your protocol)**N-AVD (preferred)**

- 6 cycles, about 6 months
- S1826: 2-yr PFS 92% vs 83% over BV-AVD
- Neutropenia; thyroid and other immune effects
- Not if autoimmune disease needs immunosuppression
- Suits all ages from 12, including over 60

BrECADD

- 4 or 6 three-week cycles (12 weeks if PET2-negative)
- HD21: better PFS than escBEACOPP; 4-yr OS 98.6%
- Febrile neutropenia 28%; transfusions common
- Fit adults ≤60 with adverse features

BV-AVD

- 6 cycles with G-CSF
- ECHELON-1: 6-yr OS 93.9% vs 89.4% over ABVD
- Neuropathy in two-thirds (mostly reversible)
- When nivolumab is contraindicated; usually ≤60

RATHL (ABVD → AVD)

- 2 ABVD, PET2; if negative, 4 AVD
- 7-yr PFS about 80%, OS 93%
- Drops bleomycin early; less lung toxicity
- When nivolumab and BV are unsuitable or unaffordable

Over 60: N-AVD, or sequential BV → AVD → BV; avoid bleomycin (ABVD in E2496: 9% treatment deaths, lung toxicity in 43%).

Figure 10. Four evidence-based starts. No trial has compared N-AVD with BrECADD; inclusion criteria and endpoints differ (S1826, HD21, ECHELON-1, RATHL; UpToDate advanced-stage review).

- **N-AVD × 6 is preferred** ([S1826](#)^[2]; 970 patients aged 12 and over): 2-year PFS 92% vs 83% over BV-AVD (HR 0.45), overall survival 99% vs 98%; fewer stopped treatment (9% vs 22%) and almost nobody needed RT (7 of 970). More grade ≥3 neutropenia (48% vs 26%); G-CSF optional. Contraindicated in autoimmune disease that needs immunosuppression.
- **Over 60:** N-AVD also worked best ([older subgroup](#)^[20]: 2-year PFS 89% vs 64%, OS 96% vs 85%), with more febrile neutropenia and infection. If N-AVD is unsuitable, sequential BV → AVD → BV ([Evans 2018](#)^[21]: 2-year PFS 84%). Avoid bleomycin over 60 ([E2496](#)^[22]: treatment deaths 9%, bleomycin lung toxicity 43%). A geriatric assessment helps; dexrazoxane can be considered for cardiac risk.
- **BrECADD** for fit adults up to 60 with adverse features ([HD21](#)^[3]; 1500 patients): better 4-year PFS than escalated BEACOPP (HR 0.66), overall survival 98.6%, fewer grade ≥3 events (42% vs 59%), and only 12 weeks of treatment after a negative PET2; but febrile neutropenia 28% and frequent transfusions. Not compared with N-AVD.
- **BV-AVD × 6 with G-CSF** when nivolumab is contraindicated ([ECHELON-1](#)^[23]: 6-year OS 93.9% vs 89.4% over ABVD; neuropathy in two-thirds, mostly reversible; no survival gain over 60).
- **RATHL** (ABVD × 2, PET2, then AVD × 4 if negative) when neither nivolumab nor BV is suitable or affordable: 7-year PFS about 80% and OS 93%.
- **Frail patients:** no standard; BV-dacarbazine, BV-nivolumab or a PD-1 inhibitor alone ([Friedberg 2024](#)^[24]), single-agent chemotherapy, steroids or palliative RT.
- **End of treatment:** PET 6–8 weeks after chemotherapy. Deauville 1–3 = complete response; 4–5 = consider biopsy, then manage as refractory.

SHARE WITH PATIENTS: TREATMENT DECISIONS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Chemotherapy is needed immediately for every lymphoma?](#)

[Radiotherapy has no role in lymphoma?](#)

[If the PET scan becomes negative, treatment can always be stopped immediately?](#)

[Immunotherapy and targeted therapy are the same as chemotherapy?](#)

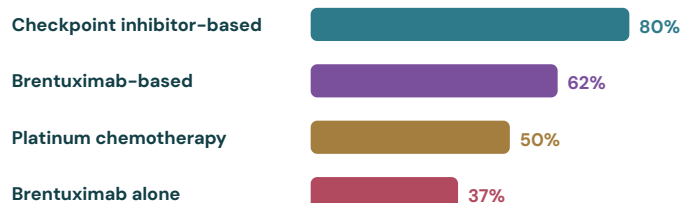
Every lymphoma needs surgery to remove the affected lymph nodes?

Relapsed or refractory classic HL

- **Who relapses:** 10–15% after early-stage and 15–25% after advanced-stage treatment. **Biopsy first:** grey-zone lymphoma, another cancer, infection, sarcoidosis or a checkpoint-inhibitor "flare" can mimic relapse.
- **Transplant-eligible:** second-line salvage, PET, then high-dose chemotherapy (usually BEAM) and autologous transplant for a complete response. Transplant is the only treatment proven to cure reliably ([Schmitz 2002](#)^[25]).
- **Choice of salvage:** if no checkpoint inhibitor was used first line, a checkpoint-based regimen (pembrolizumab–GVD, pembrolizumab–ICE, nivolumab–ICE: complete response 87–95%, 2-year PFS 88–100% after transplant; [Moskowitz 2021](#)^[26], [Bryan 2023](#)^[27], [Mei 2022](#)^[28]). BV–nivolumab is an outpatient option without anthracycline (complete response 67%; [Advani 2021](#)^[29]). After N–AVD first line, BV–based or checkpoint-based salvage are both acceptable.
- **Response before transplant matters:** 2-year PFS after transplant was 80% with checkpoint-based, 62% with BV–based and 50% with platinum salvage ([Desai 2023](#)^[30]); a complete metabolic response gave 4-year EFS 77% vs 33% ([Moskowitz 2010](#)^[31]).
- **After transplant:** BV maintenance for BV–naive patients with a high-risk feature (primary refractory or relapse within 12 months, less than complete response to salvage, B symptoms or extranodal disease at relapse, two or more salvage lines): 5-year PFS 59% vs 41% ([AETHERA](#)^[32]). RT to localised or bulky sites not previously irradiated.
- **Not transplant-eligible:** BV–nivolumab, or a PD–1 inhibitor with or without gemcitabine; then bendamustine, gemcitabine, vinblastine, lenalidomide or everolimus; RT for symptoms. PD–1 inhibitors can be stopped after about a year in complete response and restarted if needed.
- **Relapse after autologous transplant:** checkpoint inhibitor ([CheckMate 205](#)^[33]; [KEYNOTE-087](#)^[34]) or BV; reduced-intensity allogeneic transplant for fit patients with less than a complete response to a checkpoint inhibitor. Prior PD–1 blockade raises GVHD risk: post-transplant cyclophosphamide helps.

Relapse: get a complete response before the autologous transplant

2-year PFS after transplant, by salvage regimen (936 patients)



PET before transplant

- Complete metabolic response: 4-yr EFS 77%
- Anything less: 33%
- PR may still go to transplant if near-complete
- Progression: third-line first, re-biopsy

Pembrolizumab–GVD, pembrolizumab–ICE, nivolumab–ICE: complete response 87–95%, 2-year PFS 88–100% after transplant (phase 2). BV–nivolumab: outpatient, no anthracycline, complete response 67%. Transplant-ineligible: BV–nivolumab or PD–1 ± gemcitabine. Survival after autologous transplant has risen: 3-year OS 92% for 2016–2019 transplants vs 72% in the early 2000s (CIBMTR).

Figure 11. Salvage and transplant. Retrospective comparisons ([Desai 2023](#); [Moskowitz 2010](#)) and phase 2 trials quoted in the UpToDate relapsed/refractory review; no randomised trial has compared these regimens.

SHARE WITH PATIENTS: RELAPSE

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[If lymphoma returns after chemotherapy, no effective treatment remains?](#)

[CAR-T cell therapy can cure every lymphoma?](#)

Nodular lymphocyte-predominant HL (NLPHL)

NLPHL behaves like an indolent B-cell lymphoma, not like classic HL

	Classic HL	NLPHL (NLPBL in the ICC)
Share of Hodgkin lymphoma	About 95%	About 5%; 75% men; peaks in childhood and age 30–40
Malignant cell	HRS: CD30+, CD15+, CD20 weak or absent	LP ("popcorn"): CD20+, CD45+, CD30–, CD15–
Presentation	Mediastinum common; B symptoms in 40%	Slow peripheral nodes; mediastinum 2–7%; B symptoms 6–15%
Stage at diagnosis	Half or more advanced in India	About 75% stage I–II
Treatment	ABVD-based, PET-adapted; N-AVD; RT selectively	RT for IA; R-CHOP, R-CVbP or R-B; rituximab; watch
Course	Relapses mostly in the first 2–3 years	Late relapses for decades; transformation in 3–5% (7% by 10 years in one series)
Survival	Excellent if cured	Close to the general population

Excision biopsy matters most here: core needles can miss the nodular pattern that separates NLPHL from T-cell/histiocyte-rich large B-cell lymphoma.

Figure 12. Two different lymphomas. The ICC renamed NLPHL "nodular lymphocyte-predominant B-cell lymphoma"; WHO 5th edition kept NLPHL (UpToDate NLPHL reviews; GLOW, ILROG and GHSG series).

- **Diagnosis:** excision biopsy; LP cells are CD20+, CD45+, CD30– and CD15–, in nodules rich in small B cells and follicular dendritic cells. Bone marrow involvement is rare (1–2%); suspect transformation or T-cell/histiocyte-rich large B-cell lymphoma if it is found.
- **Prognosis:** LP-IPS gives one point each for age ≥45, stage III–IV, Hb <10.5 g/dL and splenic involvement ([Binkley 2024](#)^[35]); LP-IPS ≥2, or ≥1 with B symptoms or bulk over 10 cm, is higher risk.
- **Stage IA or contiguous IIA (adults):** ISRT 30–36 Gy. In the GLOW stage IA series, 6-year PFS after complete excision was 90.5% with RT vs 65.5% with watching ([Flerlage 2026](#)^[36]); in ILROG early-stage data, rituximab alone controlled the disease least well ([Binkley 2020](#)^[37]). Overall survival was excellent with every approach.
- **Children:** watch after complete excision, or R-CVbP (three cycles); RT avoided where possible ([Shankar 2012](#)^[38]).
- **Advanced or symptomatic:** chemoimmunotherapy (R-CHOP, R-CVbP or R-B, about 6 cycles; [Fanale 2017](#)^[39]); asymptomatic low-risk disease can be watched or treated with rituximab. ABVD-type regimens are no longer favoured.
- **Relapse:** always biopsy (transformation to aggressive B-cell lymphoma in about 3–5%, rising with time; [Al-Mansour 2010](#)^[40]). Asymptomatic small relapses can be watched; otherwise RT, rituximab or a different chemoimmunotherapy; transplant is rarely needed.

Children and adolescents

Children and adolescents: same disease, different priorities (growth, heart, fertility, second cancers)**Low risk**

- Stage IA/IIA, no bulk, no extranodal lesion
- ABVD × 2 then PET-guided, or OEPA × 2
- OEPA with complete response: no further treatment, no RT

Intermediate risk

- IA/IIA with bulk or E, or any IB/IIB
- ABVD (then ABVD or ABV) or ABVE-PC, PET-guided
- RT reserved for slow responders

High risk

- Stage III–IV
- N-AVD from age 12 (S1826 adolescents: 2-yr PFS 95% vs 83%)
- BV-AVD if nivolumab cannot be given; BV-AVE-PC (AHOD1331)

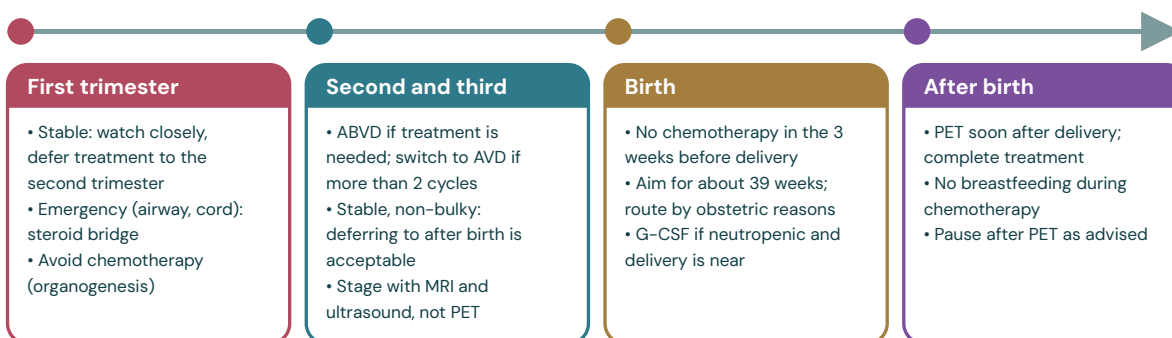
In children, "bulky" means a node mass of 6 cm or more. Treat in a paediatric oncology unit and on a protocol where possible.

India: in a 396-child prospective study, 29% had received anti-TB treatment before the biopsy, and they presented at a later stage.

Figure 13. Paediatric and adolescent cHL. Risk groups and regimens as suggested in the UpToDate paediatric review; Indian data from Mahajan 2023 (InPOG). This module summarises; paediatric protocols give the detail.

- Risk groups (no single international standard): low (IA/IIA, no bulk or extranodal lesion), intermediate (IA/IIA with bulk or E, or IB/IIB), high (III–IV). Bulk in children means a node mass of 6 cm or more.
- Low risk: ABVD × 2 then PET-guided treatment, or OEPA × 2 with no further therapy after a complete response ([GPOH-HD-2002](#)^[41]; [EuroNet-PHL-C1](#)^[42]).
- Intermediate risk: ABVD (then ABVD or ABV) or ABVE-PC, PET-guided; RT for slow responders ([AHOD0031](#)^[43]).
- High risk: N-AVD from age 12 (S1826 adolescents: 2-year PFS 95% vs 83%); BV-AVD if nivolumab cannot be used; BV-AVE-PC ([AHOD1331](#)^[44]; 3-year EFS 92% vs 83%) or AEPA-CAPDAC ([HLHR13](#)^[45]) are alternatives with more RT.
- Treat in a paediatric oncology unit, on a protocol where possible; the Indian Pediatric Oncology Group runs risk-stratified, response-adapted HL studies.

Pregnancy

Classic HL in pregnancy: the commonest cancer of pregnancy, and usually curable

Outcomes match non-pregnant patients (INCIP: 5-yr PFS about 83%, OS about 97%). Radiotherapy is avoided except for rare emergencies.

Figure 14. Pregnancy. Plan with the obstetrician and maternal-fetal medicine team; some cases are now found through abnormal prenatal cell-free DNA screening (UpToDate pregnancy review; Maggen 2019; Turriff 2024).

- cHL is the commonest cancer diagnosed in pregnancy. Symptoms (fatigue, breathlessness, anaemia) overlap with pregnancy and delay diagnosis; some cases are now found after abnormal prenatal cell-free DNA results ([Turriff 2024](#)^[46]).

- Stage with MRI without contrast and ultrasound; do not withhold necessary imaging. Plan with the obstetrician and maternal–fetal medicine specialist.
- First trimester: stable patients are watched until the second trimester; emergencies are bridged with a steroid. Second and third trimesters: ABVD (AVD if more than two cycles), or defer until after birth if stable and non-bulky. No chemotherapy in the 3 weeks before delivery; aim for about 39 weeks.
- After birth: PET, then complete treatment by the presenting stage; no breastfeeding during chemotherapy. Outcomes match non-pregnant patients ([Maggen 2019](#)^[47]; [Evans 2013](#)^[48]); children exposed to ABVD after the first trimester have done well in long-term follow-up.

People living with HIV

- cHL in HIV is almost always EBV-positive, often mixed cellularity or lymphocyte-depleted, and more often advanced or with unusual spread (marrow, liver, non-contiguous sites).
- Treat the lymphoma with standard curative regimens alongside antiretroviral therapy (S1826 allowed people living with HIV); check drug interactions and give infection prophylaxis.

India now (October 2026)

- ABVD is the established backbone: it was given to 94% of advanced-stage patients at Tata Memorial and 85% at AIIMS ([Jain 2015](#)^[4]; [Ganesan 2011](#)^[49]). Indian outcomes with ABVD-based treatment are comparable to Western series ([Bhurani 2022](#)^[1]).
- Nivolumab: the reference product is sold in India as Opdyta; the first nivolumab biosimilar (Zydus, Tishtha) was launched in January 2026 at about a quarter of the reference price, which brings N-AVD within reach of more patients.
- Low fixed doses of nivolumab, far below the licensed dose, have been used in relapsed cHL in India for cost reasons with good responses ([AIIMS, Pathak 2022](#)^[50]; CMC Vellore phase 2 with lenalidomide, [2025](#)^[51]). This is off-label and investigational; a randomised trial against ABVD in advanced disease has been started.
- Brentuximab vedotin and pembrolizumab: availability and cost in India to be confirmed by the treating team; discuss scheme or insurance cover before planning BV-AVD, BrECADD or checkpoint-based salvage.
- PET-CT is available in cities but not everywhere: when interim PET is not possible, early-stage patients should receive combined modality therapy rather than chemotherapy alone.
- Biopsy before anti-TB treatment: empirical anti-TB therapy delayed diagnosis in 16% of adults and 29% of children in Indian series.

Quick reference (also as a printable PDF on the Printable Teaching Resources page)

Table A. Diagnosis and staging tests and what they change

Test	When	What it changes	Pitfalls
Excision (or incision) node biopsy; multiple cores if not feasible	Every suspected case	Diagnosis and subtype; separates cHL from NLPHL, ALCL, PMBL, grey zone and THRLBCL	FNAC is not enough; inguinal nodes are often reactive; CT-guided or endobronchial mediastinal needles crush the tissue

Test	When	What it changes	Pitfalls
Immunohistochemistry (CD30, CD15, CD45, CD20, PAX5, BOB1/OCT2, CD3) and EBER	Every biopsy	HRS phenotype CD30+, CD15+ (75–85%), CD45–, CD3–; LP cells CD20+, CD30–, CD15–	CD15–negative cHL exists; absence of both CD15 and CD30 points elsewhere
PET-CT, skull base to mid-thigh	Staging; after 2 cycles (PET2); end of treatment	Lugano stage, bulk, marrow and extranodal disease; response–adapted decisions (Deauville)	Inflammation, infection and thymic rebound take up FDG; too early after treatment reads falsely positive
CBC, ESR, albumin, LFT, renal function, LDH	Baseline	ESR defines early–stage risk group; albumin, Hb, WBC, lymphocytes feed the IPS	Microcytic anaemia from cytokines is not iron deficiency
HBsAg, anti–HBc, HCV, HIV	Before any treatment	Antiviral prophylaxis; HIV changes management and is common in EBV–positive cases	Anti–HBc alone still needs a plan when rituximab is used (NLPHL)
Echocardiogram (LVEF)	Before anthracycline	LVEF ≥50% generally needed for doxorubicin; baseline for survivorship	Statins may slow EF decline (STOP–CA); no proven fall in heart failure
Pulmonary function with DLCO	Before bleomycin	DLCO ≥60% generally needed; repeat before extra ABVD cycles	Older age, smoking and kidney impairment raise bleomycin toxicity
Bone marrow biopsy	Only for unexplained cytopenias with a marrow–negative PET	Stage IV if involved	Homogeneous marrow uptake on PET is usually reactive
Pregnancy test; fertility counselling; sperm banking	Before treatment	Choice of regimen and timing; oocyte or tissue preservation where escalated therapy is likely	ABVD rarely causes infertility; BEACOPP–type regimens and transplant do

Table B. Treatment by setting (adults)

Setting	Usual plan	Alternatives and notes
Early favourable, PET2 Deauville 1–3, all GHSG favourable criteria	ABVD × 2 then 20 Gy involved–site RT (HD16 ^[11])	Not tested with other groups' criteria; if RT unsuitable, chemotherapy only as below
Early favourable, PET2 1–3, other criteria	Chemotherapy only: ABVD × 2 more (≤60, healthy lungs) or AVD × 2 (>60 or lung disease), up to 4 more for Deauville 3 or bulk	Or CMT: ABVD × 1 more + 30 Gy (H10 ^[52] ; fewer relapses, same survival)
Early unfavourable, PET2 1–3	CMT: ABVD × 2 more + 30 Gy ISRT, or chemotherapy only: AVD × 4 (RATHL ^[53])	Bulky mediastinum: ABVD × 6 without RT worked in CALGB 50801 ^[17] ; alternatives N–AVD, BV–AVD, BrECADD
Early stage, PET2 Deauville 4–5	ABVD × 2 or BrECADD × 2, then PET4: 1–4 → 30 Gy; 5 → biopsy	Persistent cHL on biopsy = primary refractory
Early stage, no PET available	ABVD × 3 + 30 Gy ISRT (GHSG favourable: ABVD × 2 + 20 Gy)	CMT preferred over chemotherapy only when response cannot be measured
Advanced (III–IV)	N–AVD × 6 (S1826 ^[2])	BrECADD for fit ≤60 with adverse features (HD21 ^[3]); BV–AVD if nivolumab contraindicated; RATHL when neither is possible

Setting	Usual plan	Alternatives and notes
Advanced, over 60	N-AVD; or sequential BV → AVD → BV	No bleomycin; geriatric assessment; dexrazoxane if cardiac risk; frail: BV-dacarbazine, BV-nivolumab, PD-1 alone, palliative RT
Bulky advanced disease in complete response	No consolidation RT (HDO607 ^[14])	RT for a single PET-positive residual site, or biopsy it first
First relapse or refractory, transplant-eligible	Biopsy → checkpoint-based salvage → PET complete response → autologous transplant (BEAM)	BV maintenance if BV-naïve and high risk (AETHERA ^[54]); RT to bulky unirradiated sites
Relapse, not transplant-eligible	BV-nivolumab; PD-1 inhibitor ± gemcitabine	Bendamustine, gemcitabine, vinblastine, lenalidomide, everolimus; RT for symptoms
Relapse after autologous transplant	Checkpoint inhibitor (if not already failing one); BV if not given	Allogeneic transplant (reduced intensity) for fit patients with less than CR to a checkpoint inhibitor
NLPHL stage IA or contiguous IIA	Involved-site RT 30–36 Gy (adults)	Watch after complete excision; rituximab alone relapses more; children: watch or R-CVbP
NLPHL symptomatic or higher-risk advanced	R-CHOP, R-CVbP or R-B (about 6 cycles)	Asymptomatic low-risk: watch or rituximab; biopsy every relapse (transformation)

Table C. Regimens: evidence and best fit (no doses)

Regimen	Key evidence	Best fit	Watch for
ABVD (PET-adapted)	H10 ^[52] , HD16 ^[11] , RATHL ^[53] , RAPID ^[13]	Early-stage backbone; advanced when newer drugs are unavailable (drop bleomycin after PET2-negative)	Bleomycin lung injury, neuropathy, high emetic risk (dacarbazine), vesicants (doxorubicin, vinblastine); no G-CSF or dose delays for neutropenia alone
N-AVD (nivolumab + AVD)	S1826 ^[2] : 2-yr PFS 92% vs 83% over BV-AVD; older patients 89% vs 64%	Advanced stage, age 12 and above, including over 60	Neutropenia (G-CSF optional), thyroid dysfunction, rare severe immune effects; contraindicated with active autoimmune disease on immunosuppression
BV-AVD	ECHELON-1 ^[23] : 6-yr OS 93.9% vs 89.4% over ABVD	Advanced stage when nivolumab is contraindicated; usually ≤60	Peripheral neuropathy (two-thirds), febrile neutropenia: G-CSF is mandatory
BrECADD	HD21 ^[3] : better PFS than escBEACOPP, 4-yr OS 98.6%, fewer severe AEs (42% vs 59%)	Fit adults ≤60 with advanced or high-risk stage II disease; shortest course (12 weeks if PET2-negative)	Febrile neutropenia 28%, transfusions; G-CSF every cycle
Sequential BV-AVD-BV	Evans 2018 ^[21] : 2-yr PFS 84% in patients ≥60	Older adults who cannot have N-AVD	Neutropenia, infection, neuropathy
Checkpoint-based salvage (pembrolizumab-GVD, pembrolizumab- or nivolumab-ICE)	CR 87–95%, 2-yr PFS 88–100% after transplant (phase 2 ^[26])	First relapse before autologous transplant	Immune effects; pseudoprogression or sarcoid-like reactions: biopsy before calling failure; GVHD risk if allogeneic transplant follows
BV-nivolumab	Advani 2021 ^[29] : CR 67%; 3-yr PFS 91% in transplanted patients	Outpatient salvage; transplant-ineligible patients	Neuropathy (continue nivolumab alone if it limits), infusion reactions

Regimen	Key evidence	Best fit	Watch for
BV maintenance after autologous transplant	AETHERA ^[32] : 5-yr PFS 59% vs 41%	BV-naïve patients with a high-risk feature	Neuropathy in over half, mostly reversible; neutropenia
Rituximab-based (NLPHL)	R-CHOP ^[39] , R-B, R-CVbP series	Symptomatic or higher-risk NLPHL	HBV reactivation (screen first), infusion reactions

Table D. Managing common problems during treatment

Problem	Likely cause	First steps	When to act fast
New cough, breathlessness, falling DLCO on ABVD	Bleomycin lung injury (worse with age, smoking, kidney impairment)	Stop bleomycin for good; imaging; steroids per pulmonology	Hypoxia: admit
Fever while neutropenic	Infection (more after 60, BrECADD, BV-AVD)	Febrile neutropenia protocol; G-CSF for later cycles where indicated	Hypotension, rigors: emergency
Tingling, numbness, constipation	Vinblastine or brentuximab neuropathy	Grade it each visit; dose change by protocol; laxatives	Weakness or adynamic ileus: stop the drug
Tiredness, weight change, palpitations on nivolumab	Thyroiditis (immune effect)	TSH and free T4; replace or treat	Severe diarrhoea, breathlessness, jaundice: suspect colitis, pneumonitis, hepatitis
Nodes enlarge or PET lights up early on immunotherapy	Pseudoprogression (flare) or sarcoid-like reaction	Do not stop at once; repeat imaging; biopsy if in doubt	Organ compression
Pain or swelling at the drip site	Extravasation (doxorubicin, vinblastine are vesicants)	Stop infusion; local protocol; central line for long courses	Blistering or necrosis
Severe nausea	Dacarbazine-containing regimens are highly emetogenic	Guideline antiemetics before each dose	Dehydration, kidney injury
Breathlessness or swelling years after treatment	Late cardiac effect (anthracycline, mediastinal RT)	Echo, ECG; cardiology	Chest pain, syncope
Swelling of face and arms, stridor at diagnosis	Large mediastinal mass (SVC or airway compression)	Urgent biopsy plan with anaesthetist; steroids may hamper diagnosis	Airway compromise: emergency

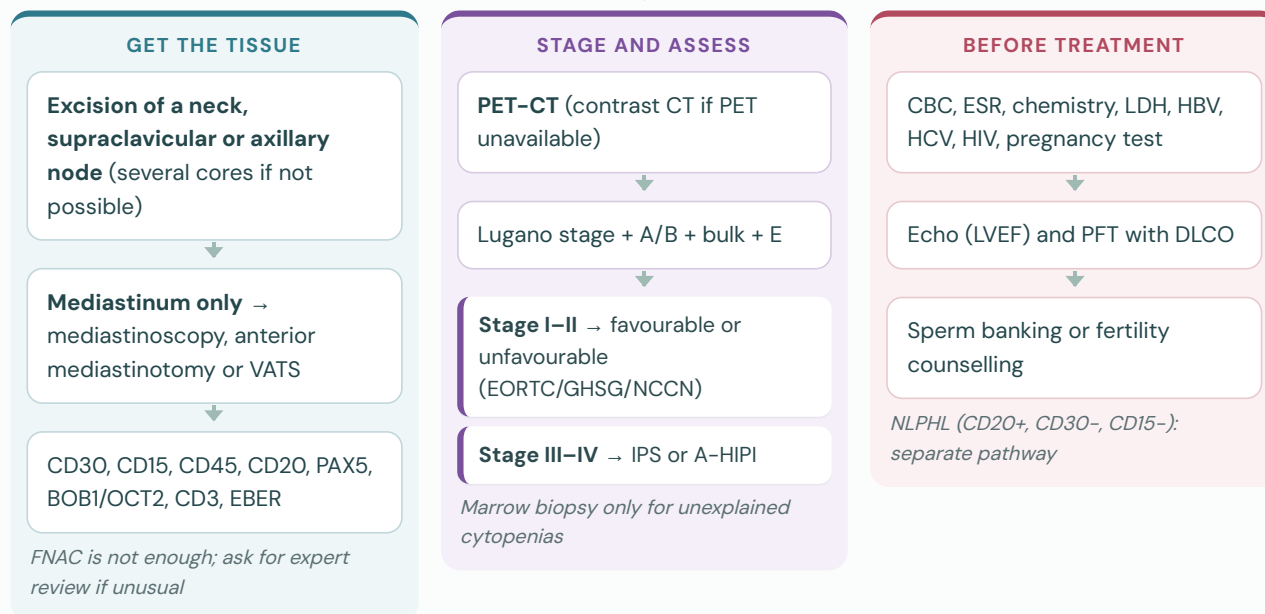
07 Management algorithms

These decision paths pull together sections 02–06. Colours: teal for favourable paths, purple for intermediate, rose for advanced or high-risk paths.

ALGORITHM 1

Suspected Hodgkin lymphoma: from a node or a mediastinal mass to a treatment group

Persistent node, mediastinal mass, or unexplained B symptoms or itch → no empirical anti-TB treatment → biopsy plan



All patients: stop smoking · vaccines before treatment · photograph and measure palpable nodes · discuss in a lymphoma multidisciplinary team.

ALGORITHM 2

Early-stage classic HL: PET-adapted ABVD

Stage I–II cHL → ABVD × 2 → PET2 (Deauville score)

FAVOURABLE, PET2 1–3

All GHSG favourable → 20 Gy ISRT, stop

Others → choose with the patient

Chemotherapy only: ABVD × 2 (≤60) or AVD × 2 (>60, lung disease); up to 4 for Deauville 3 or bulk

CMT: ABVD × 1 + 30 Gy

No PET available: ABVD × 3 + 30 Gy

UNFAVOURABLE, PET2 1–3

CMT: ABVD × 2 + 30 Gy ISRT

or chemotherapy only: AVD × 4 (no bleomycin)

Breast, heart or lung in the field, smoker → chemotherapy only; neck-only disease → CMT easier

PET2 4–5 (ANY EARLY STAGE)

Single Deauville 4 → ABVD × 2 (unfavourable: or BrECADD × 2)

PET4: **1–4** → 30 Gy; **5** → biopsy

Multiple 4 or any 5 at PET2 → biopsy first

Viable cHL on biopsy → Algorithm 4

All patients: PET at the end of treatment · visits every 3–6 months for 2 years · no routine surveillance scans · late-effect plan.

ALGORITHM 3

Advanced classic HL (stage III–IV): first-line choice

Stage III–IV → age, fitness, autoimmune disease, neuropathy, heart and lungs → access to nivolumab and BV

DEFAULT

N-AVD × 6 (age 12 and over, including over 60)

G-CSF optional; thyroid and immune-effect checks

Fit ≤60, adverse features → BrECADD is an alternative (12 weeks if PET2-negative)

Not with autoimmune disease on immunosuppression

NIVOLUMAB NOT POSSIBLE

≤60 → BV-AVD × 6 with G-CSF

Over 60 → sequential BV → AVD → BV

Neither BV nor nivolumab → RATHL: ABVD × 2, PET2, then AVD × 4

No bleomycin over 60

FRAIL OR VERY OLD

BV-dacarbazine or BV-nivolumab

PD-1 inhibitor alone

Steroids, single-agent chemotherapy, palliative RT

Goals of care; geriatric assessment

All patients: end-of-treatment PET (Deauville 4–5 → biopsy) · no RT for bulky disease in complete response · CBC yearly in follow-up · dexrazoxane if cardiac risk.

ALGORITHM 4

Relapsed or refractory classic HL

Suspected relapse or PET-positive residue → biopsy (exclude grey zone, other cancer, infection, flare) → PET

TRANSPLANT-ELIGIBLE

Salvage: checkpoint-based (pembro-GVD, pembro/nivo-ICE) or BV-nivolumab

PET CR → autologous transplant (BEAM)

PR → transplant if near-CR, else third line

Progression → third-line regimen, re-biopsy

After transplant: BV maintenance if BV-naïve and high risk; RT to bulky sites

NOT TRANSPLANT-ELIGIBLE

BV-nivolumab, or PD-1 ± gemcitabine

PET after 2–4 cycles; PD-1 up to about a year in CR

Later: bendamustine, gemcitabine, vinblastine, lenalidomide, everolimus

RT for symptomatic sites

AFTER AUTOLOGOUS TRANSPLANT

Checkpoint inhibitor (or BV if not yet used)

Less than CR, fit → reduced-intensity allogeneic transplant

Prior PD-1: higher GVHD risk; post-transplant cyclophosphamide

All patients: clinical trial where available · fertility counselling before transplant · infection prophylaxis · early palliative care when cure is no longer the aim.

o8 Survivorship, follow-up & late effects

A simple follow-up rhythm after treatment of Hodgkin lymphoma

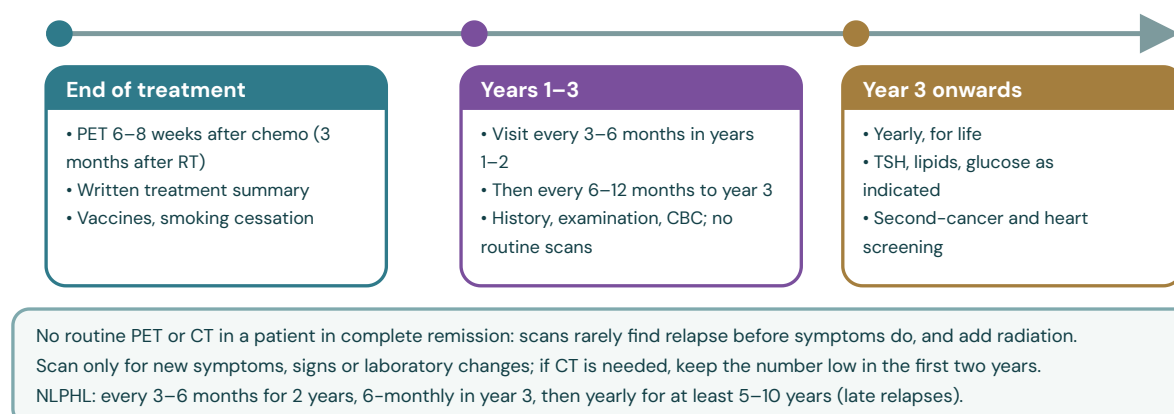


Figure 15. A simple follow-up rhythm, adapted from the UpToDate early-stage, advanced-stage, survivorship and NPLHL reviews (consistent with NCCN). Individualise by age, stage and treatment received.

- **Relapse watch:** most relapses occur in the first 2–3 years, but late relapses continue (cumulative 2.5%, 4.3% and 6.9% at 10, 15 and 20 years; [Bröckelmann 2017](#)^[55]). Biopsy any suspected late relapse: it may be NHL or a second cancer.
- **No routine surveillance PET or CT** in complete remission; image only for symptoms, signs or abnormal blood tests.
- **Laboratory follow-up:** CBC at every visit for at least 10 years; lipids yearly; TSH yearly after neck RT; glucose or HbA1c every 2 years after chest or abdominal RT.
- **Vaccines:** yearly influenza and pneumococcal vaccine; others by age and transplant history.

Late effects: what to look for, and when to start screening

Breast	Chest RT at age 10–30: yearly mammogram (consider MRI too) from age 25 or 8 years after RT, whichever is later
Heart and vessels	Cardiology review after anthracycline or chest RT; echo; carotid check after neck RT; treat BP, lipids, smoking
Lung	Baseline PFTs after chest RT ± bleomycin; low-dose CT yearly from 5 years if a heavy smoker
Thyroid	30–60% after neck RT: TSH every year
Bowel and skin	Colorectal screening 10 years earlier than usual; yearly skin check
Blood	CBC yearly; therapy-related myeloid neoplasm peaks 5–9 years (rare after ABVD)
Fertility	ABVD rarely causes infertility; alkylators do (ovarian failure 60% vs 3%); bank sperm before treatment
Mind and energy	Fatigue in a quarter to a third at 2–5 years; screen for depression and anxiety yearly

Second cancers are the leading cause of death in long-term survivors; cardiovascular disease is the leading non-cancer cause.

Figure 16. Survivorship checklist, adapted from the UpToDate survivor review (monitoring table) and second-malignancy review. Give every patient a written treatment summary: RT fields and doses, cumulative anthracycline, bleomycin.

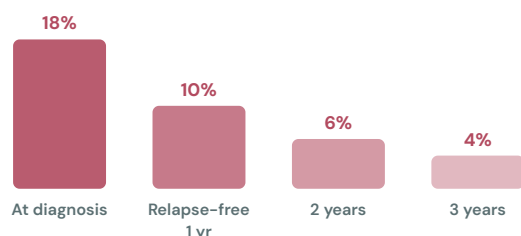
- **Second cancers** ([de Vries 2021](#)^[56]): relative risk of solid tumours 1.5–4.5-fold, starting about 5 years after treatment and rising for at least 20 years; breast, lung, colorectal, oesophageal, thyroid, skin and sarcomas,

mostly in RT fields. Doxorubicin also raises breast cancer risk independent of RT ([Neppelenbroek 2024^{\[57\]}](#)). Therapy-related AML peaks at 5–9 years after alkylators and is very rare after ABVD.

- **Heart** ([Aleman 2007^{\[58\]}](#), [van Nimwegen 2016^{\[59\]}](#), [van Nimwegen 2017^{\[60\]}](#), [Cutter 2015^{\[61\]}](#)): coronary disease, valve disease (aortic, mitral), heart failure (diastolic after RT, systolic after anthracycline), conduction problems and pericardial disease, with a median onset near 20 years. Control blood pressure, lipids, diabetes and smoking; exercise helps.
- **Lungs**: bleomycin and chest RT; smokers carry the most risk. **Thyroid**: dysfunction in 30–60% after neck RT, mostly within 5 years. **Nerves and muscles**: neuropathy after vinblastine or BV usually improves; neck-muscle weakness ("dropped head") can follow old mantle RT decades later.
- **Fertility**: ovarian function and pregnancy rates are near normal after ABVD without pelvic RT; premature ovarian failure was 60% after alkylating chemotherapy vs 3% without ([van der Kaaij 2012^{\[62\]}](#)).
- **Mind and daily life**: fatigue, anxiety and depression are common for years; survivors may face problems with work and insurance. Ask every year.

When relapses happen: mostly early, but never "never"

Risk of relapse within the next years (British Columbia, 1402 patients)



Late relapses

- No plateau: 2.5% at 10, 4.3% at 15, 6.9% at 20 years (GHSG)
- Biopsy every suspected relapse: it may be another cancer, NHL or infection

Competing risks

- In an early-stage cohort, deaths from other causes overtook Hodgkin deaths 8 years after diagnosis
- Second cancers and heart disease lead

A relapse is treatable: second-line immunotherapy-based salvage and an autologous transplant cure more than half.

Figure 17. When relapses happen (Hapgood 2016; Bröckelmann 2017; UpToDate survivorship review). Most relapses come in the first 2–3 years; follow-up then shifts towards late effects.

SHARE WITH PATIENTS: LIFE AFTER TREATMENT

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Lymphoma survivors can't return to normal life?](#)

[Lymphoma can't occur outside the lymph nodes?](#)

09 Landmark trials

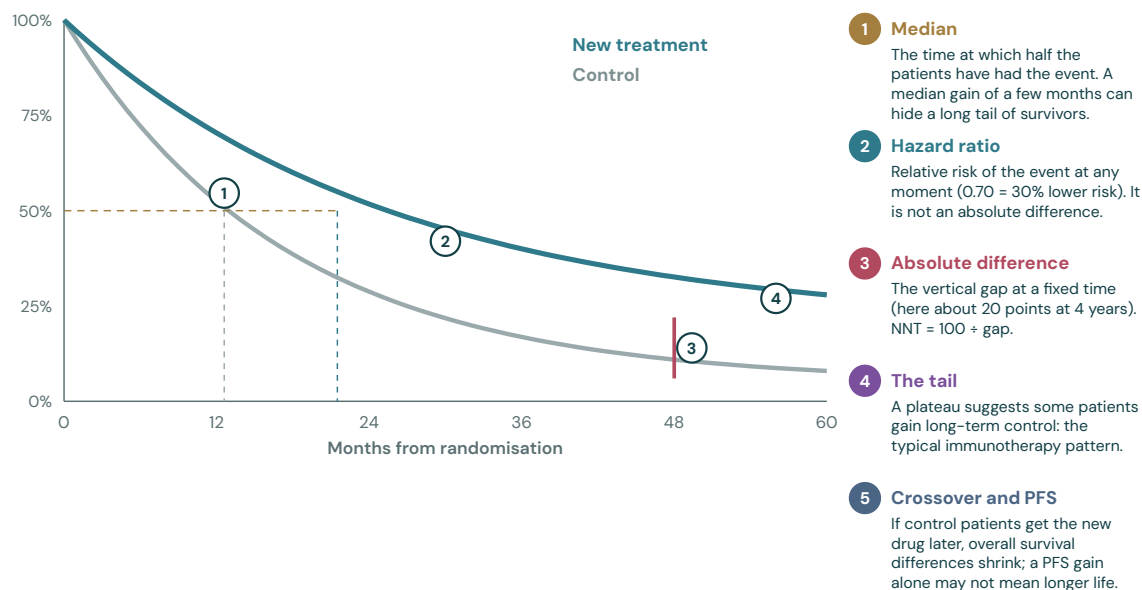
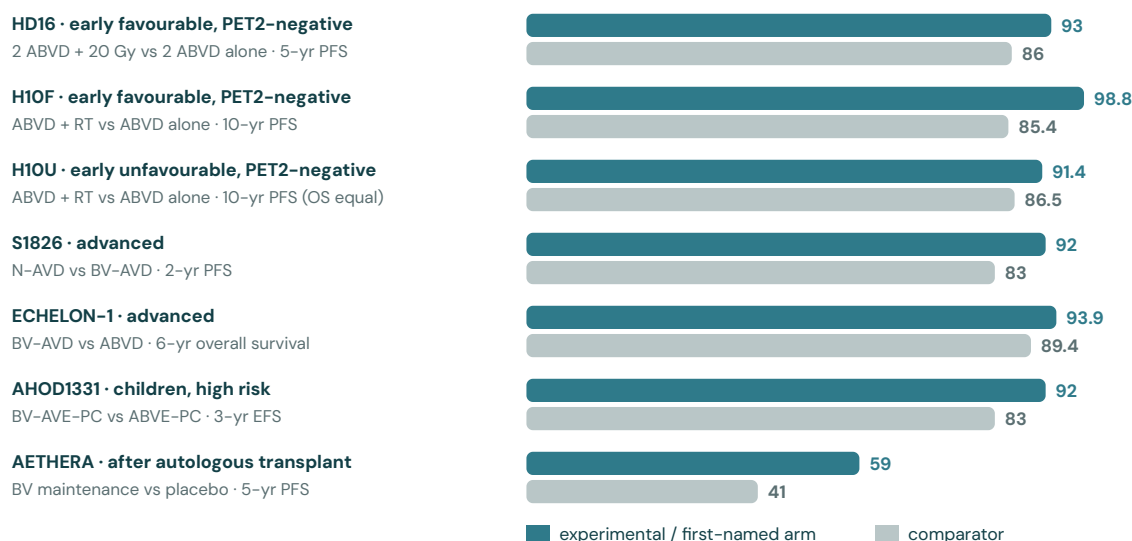


Figure 18. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

The trials behind today's choices (experimental arm vs control, %)



Endpoints and time points differ: compare arms within a trial, not across trials. In HD16 and H10 overall survival did not differ.

Figure 19. Landmark results as reported in the UpToDate reviews. Radiotherapy after a negative interim PET prevents relapses without improving survival; immunotherapy-based first-line treatment prevents relapses in advanced disease.

- **H10^[52]** and **its 10-year update^[12]**: early stage, PET2-negative → omitting RT increased relapses but not deaths → chemotherapy-only and CMT both acceptable.
- **HD16^[11]**: GHSG-favourable, PET2-negative → 20 Gy kept 5-year PFS at 93% vs 86% without RT → 2 ABVD + 20 Gy as the shortest standard.
- **RAPID^[13]**: early stage, PET-negative after 3 ABVD → RT reduced relapses without a survival difference → PET-adapted de-escalation established.

- [RATHL](#)^[53]: advanced stage, PET2-negative → AVD as good as ABVD with less lung toxicity → drop bleomycin after PET2.
- [CALGB 50801](#)^[17]: bulky early stage, PET2-negative → ABVD × 6 without RT, 3-year PFS 93% → RT not obligatory for bulk.
- [HD0607](#)^[14]: advanced stage with a large nodal mass in complete response after ABVD → no benefit from consolidation RT.
- [ECHELON-1](#)^[63] / [overall survival update](#)^[23]: BV-AVD vs ABVD in stage III–IV → 6-year OS 93.9% vs 89.4% → first survival gain in decades.
- [S1826](#)^[2]: N-AVD vs BV-AVD in stage III–IV, age 12+ → 2-year PFS 92% vs 83%, less toxicity, especially better over 60 → N-AVD preferred.
- [HD21](#)^[3]: BrECADD vs escalated BEACOPP in adults ≤60 → better PFS, less toxicity, 12-week course for most → European standard for fit young adults.
- [AHOD1331](#)^[44]: BV-AVE-PC vs ABVE-PC in high-risk children → 3-year EFS 92% vs 83%.
- [GHSG/EBMT](#)^[25]: high-dose therapy and autologous transplant vs conventional salvage in chemosensitive relapse → better freedom from treatment failure (55% vs 34% at 3 years) → transplant as the curative standard.
- [AETHERA](#)^[54]: BV maintenance after transplant in high-risk patients → 5-year PFS 59% vs 41%.

10 Practice pearls & pitfalls

- A painless, rubbery neck node that persists for more than a few weeks needs an excision biopsy, not empirical anti-TB treatment.
- A granuloma on a small sample does not exclude Hodgkin lymphoma: about 15% of cHL nodes contain granulomas.
- FNAC can raise the suspicion but cannot make the diagnosis; ask the surgeon for the whole node.
- Itch and pain after alcohol are not B symptoms, but they are real clues.
- Record the ESR before treatment: in early-stage disease it decides the risk group.
- Check DLCO before bleomycin and stop bleomycin at the first sign of lung injury; it is not needed after a negative PET2 in advanced disease.
- Do not delay ABVD or cut doses for neutropenia alone, and do not give routine G-CSF with it.
- Use only the GHSG criteria to select patients for 2 ABVD + 20 Gy.
- A negative PET2 lets you omit RT at the cost of a few more relapses, not of survival: share that choice with the patient.
- Time the end-of-treatment PET for 6–8 weeks after chemotherapy; earlier scans over-read inflammation.
- A new PET-avid spot on a checkpoint inhibitor may be a flare or a sarcoid-like reaction: biopsy before you change treatment.
- In relapse, aim for a complete metabolic response before the autologous transplant.
- Over 60, avoid bleomycin and think about N-AVD first.
- NLPHL is a different disease: CD20-positive, indolent, late relapses; treat it like an indolent B-cell lymphoma.
- Give every survivor a written treatment summary: RT fields and doses, anthracycline total, bleomycin, and a screening plan for breast, heart, thyroid and lung.

11 Case vignettes: lines of management

CASE 1 Early favourable · after empirical anti-TB treatment

Four months of anti-TB tablets for a neck node

24 years, woman

Left cervical nodes

ESR 18

A 24-year-old teacher noticed a painless lump in the left side of her neck. FNAC elsewhere was "reactive, ?granulomatous"; she took anti-TB treatment for 4 months but the node grew to 3 cm. She has no fever, sweats or weight loss.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

DIAGNOSE

Excision of the node: nodular sclerosis cHL (CD30+, CD15+, CD45-, CD20-); EBER negative. Stop anti-TB drugs.

2

STAGE

PET-CT: left upper and lower cervical nodes only (one region), no mediastinal disease. Stage IA. ESR 18, no bulk, no extranodal disease: favourable by GHSG, EORTC and NCCN.

3

BEFORE TREATMENT

Echo, PFT with DLCO, HBV, HCV, HIV, pregnancy test; fertility counselling (ABVD rarely affects fertility).

4

TREAT

ABVD × 2 → PET2 Deauville 2. She meets every GHSG favourable criterion: 20 Gy ISRT to the left neck, then stop. Neck-only RT spares breast and heart; TSH yearly afterwards.

TEACHING POINTS

- Biopsy before anti-TB treatment; granulomas occur in cHL.
- Only GHSG-favourable patients qualify for 2 ABVD + 20 Gy (HD16).
- Neck RT means yearly TSH for life.

See: Sections 02, 03 and 06, Algorithms 1 and 2.

CASE 2 Early unfavourable · bulky mediastinum

Cough and a wide mediastinum on a chest X-ray

30 years, man

Mediastinal mass 11 cm

Night sweats

A 30-year-old software engineer has 3 months of dry cough, drenching night sweats and 4 kg weight loss. Chest X-ray: anterior mediastinal mass. CT: 11 cm mass (mediastinal ratio 0.4) and right supraclavicular nodes. He smokes 10 cigarettes a day.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

GET TISSUE

Supraclavicular node excision (easier than mediastinoscopy): nodular sclerosis cHL. Anaesthetist reviews the airway first.

2

STAGE AND GROUP

PET-CT: stage IIB with bulky mediastinal disease, ESR 62: early unfavourable.

3

BEFORE TREATMENT

Sperm banking; DLCO 82%; echo normal; smoking cessation.

4

TREAT

ABVD × 2 → PET2 Deauville 3. Options explained: CMT (ABVD × 2 + 30 Gy to the mediastinum, heart and lungs in the field) or AVD × 4 without RT. He chooses AVD × 4 (RATHL, CALGB 50801). End-of-treatment PET Deauville 2.

TEACHING POINTS

- Bulky mediastinum and B symptoms make stage II unfavourable.
- After a negative PET2, chemotherapy only is acceptable even for bulk; RT adds relapse protection, not survival.
- Drop bleomycin after PET2 to protect the lungs of a smoker.

See: Sections 03, 05 and 06, Figure on radiotherapy, Algorithm 2.

CASE 3 Advanced · N-AVD · India access**Fever, weight loss and nodes on both sides of the diaphragm**

38 years, man

Stage IVB

IPS 4

A 38-year-old farmer from a nearby district has 2 months of evening fever, weight loss of 9 kg and itching. Examination: cervical and inguinal nodes, spleen tip palpable. Hb 9.8 g/dL, albumin 3.1 g/dL, WBC 16,000, ESR 98. He was given anti-TB treatment for 6 weeks without improvement.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

DIAGNOSE

Cervical node excision: mixed cellularity cHL, EBER positive. HIV negative; HBsAg negative, anti-HBc negative.

2

STAGE

PET-CT: nodes above and below the diaphragm, spleen and multifocal bone marrow uptake: stage IVB. IPS 4 (albumin, Hb, male, stage IV; WBC 16,000 adds a fifth point).

3

CHOOSE

No autoimmune disease: N-AVD × 6. Cost discussed: nivolumab biosimilar makes it affordable under his scheme. If not, RATHL (ABVD × 2, PET2, AVD × 4) is the fallback.

4

MONITOR

TSH every few cycles; G-CSF after a febrile episode; end-of-treatment PET Deauville 1. Follow-up every 3 months in year 1.

TEACHING POINTS

- Mixed cellularity, EBV positivity and stage IV with B symptoms are the typical Indian picture.
- IPS counts: albumin <4, Hb <10.5, male, age >45, stage IV, WBC ≥15,000, lymphopenia.
- N-AVD is preferred; RATHL remains a sound option when access is limited.

See: Sections 01, 03 and 06, Algorithm 3.

CASE 4 Older adult · no bleomycin**A 67-year-old with diabetes and COPD**

67 years, woman

Stage IIIA

COPD, diabetes

A 67-year-old retired nurse has painless axillary and para-aortic nodes. She has COPD (DLCO 55%), type 2 diabetes and hypertension; she walks a kilometre daily and manages her household.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

ASSESS

Biopsy: nodular sclerosis cHL. PET-CT: stage IIIA. Geriatric assessment: fit. Echo: LVEF 58%.

2

CHOOSE

No bleomycin (DLCO 55%, age over 60). N-AVD × 6 (S1826 older subgroup: 2-year PFS 89% vs 64% over BV-AVD). G-CSF for febrile neutropenia risk; dexrazoxane discussed.

3

IF NIVOLUMAB WERE UNSUITABLE

Sequential BV → AVD → BV, or AVD alone; avoid ABVD (E2496: treatment deaths 9%).

4

FOLLOW-UP

Glucose control during steroid antiemetics; TSH; end-of-treatment PET Deauville 2.

TEACHING POINTS

- Over 60, bleomycin causes more harm than benefit.
- N-AVD worked especially well in older adults, with more infections: plan G-CSF and early review of fever.
- Fitness, not age alone, decides intensity.

See: Section O6 (advanced, over 60), Algorithm 3.

CASE 5 Primary refractory · transplant**PET still positive after six cycles**

26 years, man

Stage IIIB

Deauville 5

A 26-year-old completed ABVD × 2 then AVD × 4 for stage IIIB cHL (PET2 was Deauville 3). End-of-treatment PET shows a Deauville 5 mediastinal mass and a new para-aortic node.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

CONFIRM

Biopsy of the para-aortic node: viable cHL, not grey-zone lymphoma or infection. Primary refractory disease.

2

SALVAGE

Pembrolizumab-GVD (or nivolumab-ICE): PET after 4 cycles Deauville 2. Sperm already banked.

3

TRANSPLANT

BEAM and autologous transplant. High-risk features (primary refractory) and BV-naïve: BV maintenance (AETHERA). RT to the bulky mediastinal site discussed.

4

IF HE RELAPSES AGAIN

Checkpoint inhibitor or BV; reduced-intensity allogeneic transplant if less than a complete response.

TEACHING POINTS

- Always biopsy before calling it refractory.
- Checkpoint-based salvage gives the most complete responses; get a complete response before transplant.
- BV maintenance helps BV-naïve high-risk patients after transplant.

See: Section O6 (relapse), Figure on salvage, Algorithm 4.

CASE 6 Pregnancy**Neck nodes at 10 weeks of pregnancy**

27 years, woman

10 weeks pregnant

Stage IIA

A 27-year-old in her first pregnancy has a 2.5 cm right neck node and a small mediastinal mass on a shielded chest X-ray. She has no symptoms and no breathing difficulty.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 DIAGNOSE

Excision biopsy under local anaesthesia: nodular sclerosis cHL.

2 STAGE WITHOUT PET

MRI chest–abdomen–pelvis without contrast and neck ultrasound: right neck and non-bulky mediastinal disease, stage IIA.

3 PLAN

Stable in the first trimester: watch closely and start ABVD in the second trimester (AVD after 2 cycles). Joint care with obstetrics and maternal–fetal medicine. No chemotherapy in the 3 weeks before delivery; aim for about 39 weeks.

4 AFTER BIRTH

PET soon after delivery: Deauville 2 → complete treatment as early-stage disease; no breastfeeding during chemotherapy.

TEACHING POINTS

- Defer treatment through the first trimester if the disease allows.
- ABVD in the second and third trimesters is the best-studied option.
- Outcomes for mother and child are comparable to non-pregnant patients.

See: Section O6 (pregnancy), Figure on pregnancy.

CASE 7 NLP HL

A neck node that has been there for two years

35 years, man

Single cervical node

No B symptoms

A 35-year-old accountant has a slowly enlarging, painless 3 cm left cervical node first noticed two years ago. He feels well.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 DIAGNOSE

Excision: nodular growth pattern with LP ("popcorn") cells, CD20+, CD45+, CD30–, CD15–; background small B cells and CD57+ T-cell rosettes: NLP HL. Expert review excludes T-cell/histiocyte-rich large B-cell lymphoma.

2 STAGE

PET-CT: one involved region, stage IA; LP-IPS O.

3 TREAT

ISRT 30 Gy to the left neck (better control than watching or rituximab alone in GLOW and ILROG data). Watching would have been reasonable had the node been completely excised and he preferred to avoid RT.

4 FOLLOW-UP

Every 3–6 months for 2 years, then 6-monthly, then yearly for at least 10 years; biopsy any relapse (transformation).

TEACHING POINTS

- NLPHL is CD20–positive and indolent: different from cHL.
- Stage IA disease in adults: RT is the usual choice.
- Late relapses and transformation mean long follow-up.

See: Section O6 (NLPHL), Figure on NLPHL.

12 References & guidelines

- NCCN Guidelines: Hodgkin Lymphoma (current version); ESMO Lymphomas clinical practice guideline (2025); British Society for Haematology guideline for the first-line management of classical Hodgkin lymphoma (2022); BCSH guideline on NLP HL (2016); ILROG field and dose guidelines (2014) and involved-site RT overview (2020); [Lugano 2014](#)^[7]; ICMR consensus document for paediatric lymphomas (2017); WHO Classification, 5th edition, and the International Consensus Classification (2022).
- Cross-checked in October 2026 against 15 UpToDate topic reviews: cHL presentation, evaluation and diagnosis; pretreatment evaluation, staging and stratification; favourable early-stage cHL; unfavourable early-stage cHL; advanced-stage cHL; relapsed or refractory cHL; haematopoietic cell transplantation in cHL; NLP HL clinical manifestations, diagnosis and staging; NLP HL treatment; HL in children and adolescents; cHL during pregnancy; the adult survivor of cHL; second malignancies after cHL; cardiotoxicity of radiotherapy for HL; society guideline links. The classification topic was used for naming.
- Separate UpToDate topics on Hodgkin lymphoma in older adults and in people living with HIV were not available: those parts rest on the advanced-stage, early-stage, presentation and survivorship reviews.
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FURTHER READING (NOT CITED IN THE TEXT ABOVE)

- **Post-ASCT survival in the novel-agent era (Shah 2022):** Shah H, Jang H, Singh P, et al. Improved post-ASCT survival of relapsed/refractory classical Hodgkin lymphoma patients in the era of novel agents. *Leuk Lymphoma* 2022;63:813. [PubMed](#) **Relapse and transplantation**
- **NLPHL in GHSG trials (Eichenauer 2020):** Eichenauer DA, Plütschow A, Fuchs M, et al. Long-term follow-up of patients with NLPHL treated in the HD7 to HD15 trials (GHSG). *J Clin Oncol* 2020;38:698. [PubMed](#) **NLPHL**
- **Relapse risk over time (Hapgood 2016):** Hapgood G, Zheng Y, Sehn LH, et al. Evaluation of the risk of relapse in classical Hodgkin lymphoma at event-free survival time points. *J Clin Oncol* 2016;34:2493. [PubMed](#) **Late effects and survivorship**

Educational summary for health professionals, written in our own words from current guidelines and primary trials. No drug doses are given. Non-Hodgkin lymphomas and leukaemias will follow as separate modules in the haematological cancers series. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.