

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Aggressive B-cell Lymphomas

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

Dr. Haritha Chiramana

MD (Internal Medicine), DM (Medical Oncology)
Senior Medical Oncologist & Hemato-Oncologist
C.R. Reddy Cancer Center, C.R. Reddy Superspeciality Hospital
17/406, Old Post Office Road, near Leela Mahal Road, Nellore, Andhra Pradesh 524003
Phone 0861 232 5344 · WhatsApp +91 79896 42272
info@drharitha.co.in · drharitha.co.in

Dr. Haritha teaches oncology to postgraduates and medical students. Colleges and departments may write to info@drharitha.co.in for teaching sessions.

CONTENTS

- | | |
|---|---|
| 01 At a glance | 07 Management algorithms |
| 02 Clinical presentation, common traps & causes | 08 Survivorship, follow-up & late effects |
| 03 Diagnosis, workup & staging essentials | 09 Landmark trials |
| 04 Biology and biomarkers that change treatment | 10 Practice pearls & pitfalls |
| 05 Local therapy: radiotherapy & surgery | 11 Case vignettes: lines of management |
| 06 Systemic therapy: indications & options | 12 References & guidelines |

Cite as: Chiramana H. Aggressive B-cell Lymphomas: a mini review for clinicians. Oncology Knowledge Hub [Internet]. Nellore (India): drharitha.co.in; 2026 [updated 2026 Oct 16]. Available from: <https://drharitha.co.in/professionals/aggressive-b-cell-lymphomas> · Free for education with attribution (CC BY-NC-ND 4.0).

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.

Aggressive B-cell Lymphomas

Haematological cancers, part 2 · DLBCL and high-grade B-cell lymphoma · Primary mediastinal, Burkitt and primary CNS lymphoma · R-CHOP and Pola-R-CHP · CNS risk · CAR-T and bispecific antibodies · HIV, PTLD and Richter · Survivorship · Key points for clinicians · Last updated 16 October 2026

01 At a glance

- **Diffuse large B-cell lymphoma (DLBCL) is the commonest lymphoma**, about one in four of all non-Hodgkin lymphomas worldwide and the most common in Asia. Burkitt lymphoma, primary mediastinal, high-grade (double-hit) and primary CNS lymphoma are smaller members of the same aggressive family.
- **It grows over weeks**: a rapidly enlarging node or extranodal mass, B symptoms in one in three and a raised LDH in more than half. About 60% have stage III–IV disease.
- **The diagnosis needs tissue architecture**: an excision or incision biopsy (or several cores), immunohistochemistry for cell of origin and FISH for *MYC*, *BCL2* and *BCL6*. FNA is not enough.
- **R-CHOP cures about two in three** ([GELA^{\[1\]}](#), [MinT^{\[2\]}](#)). Pola-R-CHP improves progression-free survival, mostly in non-GCB disease ([POLARIX^{\[3\]}](#)). Low-risk limited-stage disease needs only four cycles.
- **Entity matters more than stage in some cases**: Burkitt lymphoma needs intensive, CNS-directed treatment; primary CNS lymphoma needs high-dose methotrexate; people living with HIV, transplant recipients and patients with Richter transformation each need their own plan.
- **Relapse is no longer the end**: CD19 CAR-T improves survival after early relapse ([ZUMA-7^{\[4\]}](#)) and bispecific antibodies help those who cannot have it. India now makes its own CAR-T (NexCAR19, 2023).
- **Event-free at two years usually means cured**: survival then approaches that of the general population ([Maurer 2014^{\[5\]}](#)). Survivors need lifelong heart and second-cancer care.
- **India traps**: hepatitis B must be checked before rituximab; G6PD deficiency matters before rasburicase; and many patients first receive anti-TB treatment or steroids before a biopsy.

Aggressive B-cell lymphomas: one family, several diseases, one goal (cure)

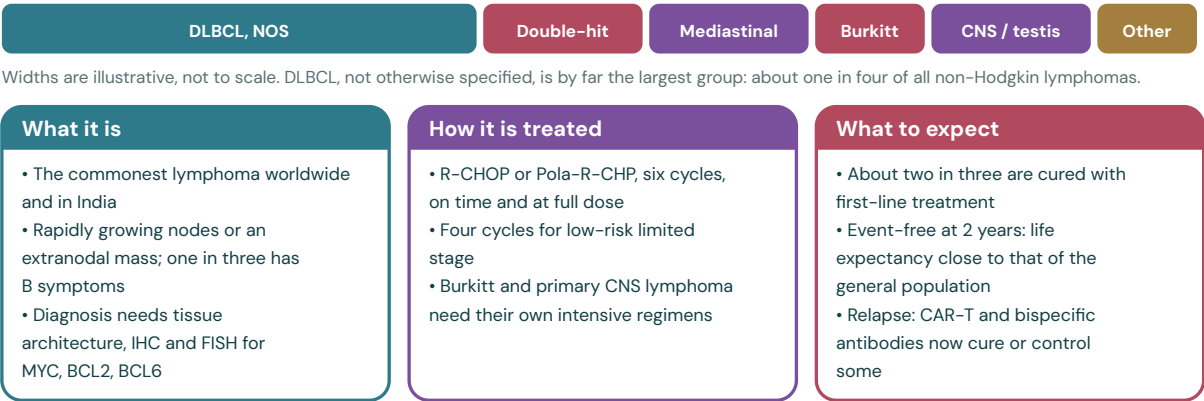
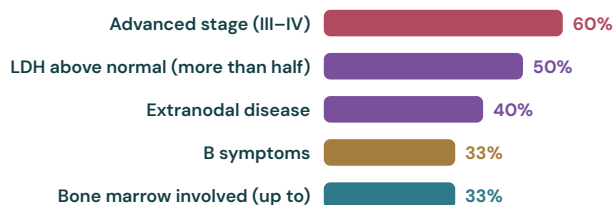


Figure 1. Aggressive B-cell lymphomas at a glance. Outcome figures from the UpToDate DLBCL prognosis and advanced-stage treatment reviews and the EFS24 analysis (Maurer 2014). Each entity is described in sections 02–06.

02 Clinical presentation, common traps & causes

How DLBCL presents at diagnosis



Emergencies at presentation

- Superior vena cava or airway compression
- Spinal cord compression
- Tumour lysis, high calcium, kidney obstruction
- Leptomeningeal or brain disease

Extranodal sites: stomach and gut most often; also testis, bone, thyroid, Waldeyer's ring and tonsil, salivary glands, skin, breast, liver, kidney and adrenal, sinuses, orbit, uterus and CNS. Marrow histology may be discordant (small cells: an undiagnosed follicular lymphoma).

Indolent past? Waxing and waning nodes for years, then sudden growth, B symptoms or a rising LDH suggests transformation.

Ask about HIV risk, transplant or immunosuppression, CLL, and a family history of lymphoma (relatives have about 3.5-fold risk).

Figure 2. Presentation. Percentages from the UpToDate DLBCL presentation and NHL initial-evaluation reviews (approximate; the advanced-stage review quotes two-thirds with stage III–IV).

Who gets it, and why

- **Age and sex:** DLBCL rises with age (median 64 in the United States) and is slightly more common in men (about 55%). In low- and middle-income countries patients present younger and with more advanced disease.
- **India:** Roche India estimates about 25,000 new DLBCL diagnoses a year. In an elderly cohort at Tata Medical Center, Kolkata, five-year overall survival was 44%; anthracycline- and rituximab-based treatment did better, and half the patients needed a steroid pre-phase ([Sarker 2021^{\[6\]}](#)).
- **Immune deficiency:** HIV (DLBCL and Burkitt are AIDS-defining), organ or stem-cell transplantation (PTLD), and long-term immunosuppression (for example methotrexate) raise the risk; EBV drives many of these lymphomas.
- **Transformation:** DLBCL can arise from follicular lymphoma, marginal zone lymphoma or CLL (Richter transformation). Years of waxing and waning nodes followed by sudden growth suggest it.
- **Family:** relatives of people with an aggressive lymphoma have about a 3.5-fold higher risk of lymphoma. Lymphoma is not contagious.
- **Children:** Burkitt and DLBCL are among the commonest childhood lymphomas; Burkitt is about 30% of childhood non-Hodgkin lymphoma in non-endemic regions.

Common traps

- **Steroids before the biopsy.** They shrink the node and can make the biopsy non-diagnostic. Biopsy first, unless an airway or cord emergency forces your hand.
- **FNA reported as "lymphoproliferative" or "reactive".** FNA can neither diagnose nor exclude lymphoma; ask for the whole node or several cores.
- **Weeks of anti-TB treatment or antibiotics for a growing node.** A node that grows over 4–6 weeks, or is larger than 2 cm, needs a biopsy.

- **An abdominal mass in a child or young man taken for appendicitis or intussusception.** Think Burkitt: send fresh tissue and check uric acid, potassium and creatinine.
- **A mediastinal mass in a young woman** with morning facial swelling: primary mediastinal lymphoma until proven otherwise; ask the anaesthetist to review the airway before any procedure.
- **Missing the double-hit.** Without *MYC* FISH, a high-grade B-cell lymphoma with *MYC* and *BCL2* rearrangements is called DLBCL and under-treated.
- **Missing hepatitis B.** Reactivation on rituximab can cause fatal hepatitis; anti-HBc alone is enough to need a plan.

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?

Lymphoma can't occur outside the lymph nodes?

03 Diagnosis, workup & staging essentials

Making the diagnosis

- **Tissue:** excision or incision biopsy of the most accessible abnormal node (neck, axilla rather than groin), or several cores; fresh tissue for flow cytometry when possible. Review by an expert haematopathologist improves accuracy and can change management.
- **Morphology and phenotype:** sheets of large cells (centroblasts or immunoblasts), Ki-67 usually above 40%; CD19, CD20, CD22, CD79a positive. CD30 in 10–20% (more favourable), CD5 in a few (worse).
- **Cell of origin:** GCB or non-GCB (activated B-cell) by the Hans algorithm (CD10, BCL6, MUM1; [Hans 2004](#)^[7]) or gene-expression profiling.
- **Genetics:** FISH for *MYC*; if rearranged, for *BCL2* and *BCL6*. Two classifications ([WHO5](#)^[8] and [ICC](#)^[9]) name the entities slightly differently, but both separate *MYC* + *BCL2* rearranged lymphoma from DLBCL, NOS.

The large B-cell family: what makes each entity different

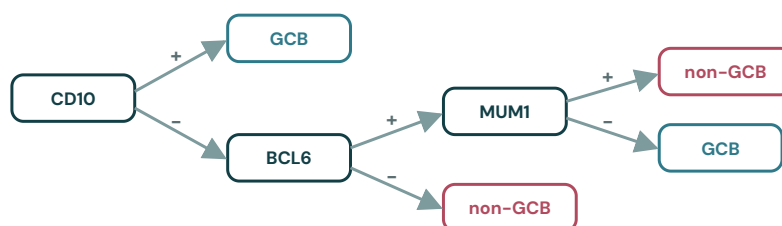
DLBCL, NOS Sheets of large cells; GCB or ABC by cell of origin	HGBL with <i>MYC</i> + <i>BCL2</i> Both genes rearranged on FISH ("double-hit"); worse with R-CHOP	Primary mediastinal Adolescents and young adults, more often women; anterior mediastinum	Burkitt lymphoma <i>MYC</i> with an Ig partner; Ki-67 near 100%; starry sky
Primary CNS / testis "Immune-privileged" sites (WHO5); CNS-penetrating treatment	PCDLBCL, leg type Nodules on the lower leg, older women; skin only on PET	EBV-positive DLBCL More common in Asia (8–10% of DLBCL); mostly extranodal	T-cell/histiocyte-rich Fewer than 10% tumour cells; mimics Hodgkin
Plasmablastic CD20-negative, CD138-positive; mouth; HIV; EBV+	Intravascular LBCL Cells inside small vessels; CNS, skin, fever; no mass	Primary effusion HHV-8 in every case; pleural or peritoneal fluid; HIV	ALK-positive LBCL Very rare; CD20-negative; poor prognosis

Double-expressor DLBCL (*MYC* and *BCL2* protein on IHC, no rearrangements) stays within DLBCL, NOS: higher risk, but not a separate entity.

Figure 3. The large B-cell lymphoma family in the WHO 5th edition and the International Consensus Classification (names differ slightly; details in the UpToDate DLBCL classification review).

From the biopsy to a complete diagnosis

Cell of origin: Hans algorithm (positive = ≥30% of cells)



Order on every case

- CD20, CD19, CD79a, CD10, BCL6, MUM1, Ki-67
- *MYC* and *BCL2* IHC; CD5, CD30
- FISH: *MYC*, then *BCL2* and *BCL6* if *MYC* is rearranged
- EBER (EBV); HHV-8 if an effusion

Tissue: excision or incision biopsy preferred; several cores if not possible. FNA can neither diagnose nor exclude lymphoma.

Biopsy before steroids. *MYC* FISH even when *MYC* staining is low: some mutations hide the epitope. Some centres reserve FISH for *MYC* IHC above 40%.

IHC agrees with gene-expression profiling in about 80%; cell of origin is prognostic and helps choose Pola-R-CHP, but is not essential to start.

Figure 4. Pathology work-up (Hans 2004; UpToDate DLBCL diagnosis and prognosis reviews). Review by an expert haematopathologist improves diagnostic accuracy.

Before treatment

Area	What to do	Why
History and examination	B symptoms, node regions, liver and spleen, neurological examination, performance status, comorbidities, prior CLL or follicular lymphoma, HIV and transplant history	Stage, IPI, fitness, CNS risk, entity
Blood tests	CBC with differential; electrolytes, uric acid, phosphate, calcium, creatinine, liver tests, LDH	IPI; tumour lysis risk
Viruses	HBsAg and anti-HBc (HBV DNA if either is positive), HCV, HIV	Antiviral prophylaxis; HIV changes the regimen and supportive care
Heart	Echocardiogram or MUGA before an anthracycline	LVEF below 40%: replace doxorubicin
Imaging	PET-CT neck to pelvis; contrast CT if PET is not available or for vessel or bowel detail; MRI brain if neurological signs	Lugano stage; baseline for end-of-treatment PET
CNS	CNS-IPI for everyone; MRI and lumbar puncture with flow cytometry for symptoms, high CNS-IPI, testicular or kidney/adrenal disease, double-hit; always in Burkitt	CNS-directed treatment
Bone marrow	Not needed if PET shows marrow disease; optional otherwise; consider for unexplained cytopenias	Discordant small-cell involvement suggests transformation
Fertility and pregnancy	Pregnancy test; sperm banking; ovarian options before intensive regimens	R-CHOP usually spares fertility; repeated lines and transplant do not
Older adults	Simplified geriatric assessment (ADL, IADL, comorbidity score) or gait speed and grip strength	Fit, unfit or frail: decides R-CHOP versus R-mini-CHOP (Merli 2021^[10])

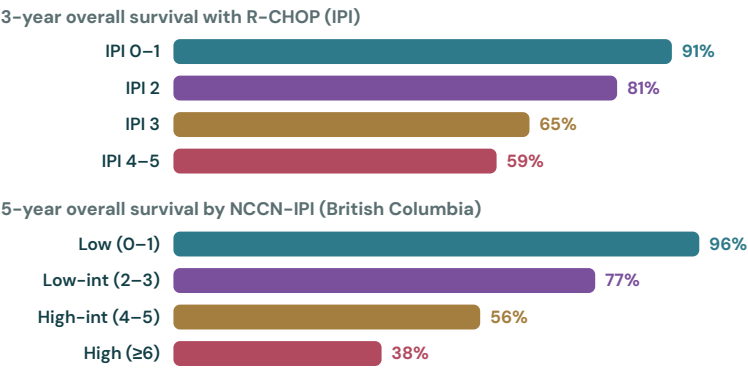
Staging and prognosis

- Lugano staging ([Cheson 2014^{\[11\]}](#)): stage I–II = limited, III–IV = advanced; extent by PET-CT. Bulky stage II behaves like advanced disease in older series.
- The International Prognostic Index ([IPI 1993^{\[12\]}](#)) remains valid with R-CHOP ([Ziepert 2010^{\[13\]}](#)); the NCCN-IPI separates groups better ([Zhou 2014^{\[14\]}](#)).
- Every patient also gets a CNS-IPI score (section 04).

Prognosis at diagnosis: the IPI still works in the rituximab era

IPI: one point each

- Age over 60
- LDH above normal
- ECOG performance status 2 or more
- Stage III or IV
- More than one extranodal site



NCCN-IPI treats age and LDH as graded values and counts marrow, CNS, liver/gut and lung disease: it separates groups better but is harder at the bedside.
Age-adjusted IPI (stage, LDH, performance status) is used for patients 60 or younger; a stage-modified IPI for stage I-II disease.

Figure 5. Prognostic indices. Survival from Ziepert 2010 (1063 patients, R-CHOP or CHOP-like) and Zhou 2014 (NCCN-IPI validation cohort), as quoted in the UpToDate prognosis review.

SHARE WITH PATIENTS: SCANS, BIOPSIES AND THE TYPE OF LYMPHOMA

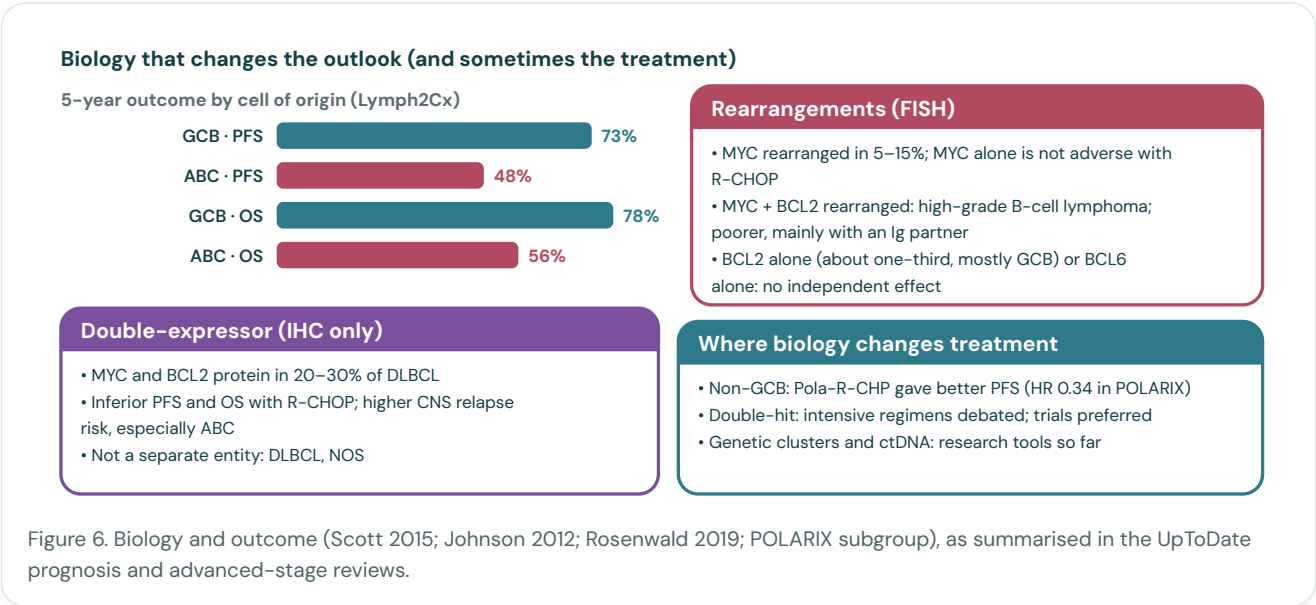
Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

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

[A lymph node that lights up on PET always means cancer?](#)
- [All lymphomas are the same cancer?](#)

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

04 Biology and biomarkers that change treatment



Marker or feature	What it tells you	What it changes
Cell of origin (GCB vs non-GCB)	Non-GCB (ABC) has more relapses with R-CHOP (Scott 2015 ^[15])	Favours Pola-R-CHP when affordable; prognostic otherwise
MYC + BCL2 rearrangement (FISH)	High-grade B-cell lymphoma; worse with R-CHOP, mainly when MYC's partner is an immunoglobulin gene (Rosenwald 2019 ^[16])	More intensive regimens are often used; CNS work-up; trial
MYC and BCL2 protein (IHC, "double-expressor")	20–30% of DLBCL; poorer outcome and more CNS relapse (Johnson 2012 ^[17])	Not a separate entity; trigger for FISH
CD20	Target of rituximab; absent in plasmablastic, ALK-positive and primary effusion lymphoma	No rituximab if CD20-negative
CD19	Target of CAR-T and some antibodies	Re-check at relapse before CAR-T
CD30	Present in 10–20%; more favourable	Research target
EBV (EBER)	EBV-positive DLBCL; HIV, PTLD, chronic inflammation	Look for immune deficiency; reduce immunosuppression in PTLD
Circulating tumour DNA	End-of-treatment ctDNA predicts relapse better than PET in studies (Roschewski 2025 ^[18])	Not yet standard

Who is at risk of CNS relapse? (3.4% of DLBCL in a Danish national cohort)

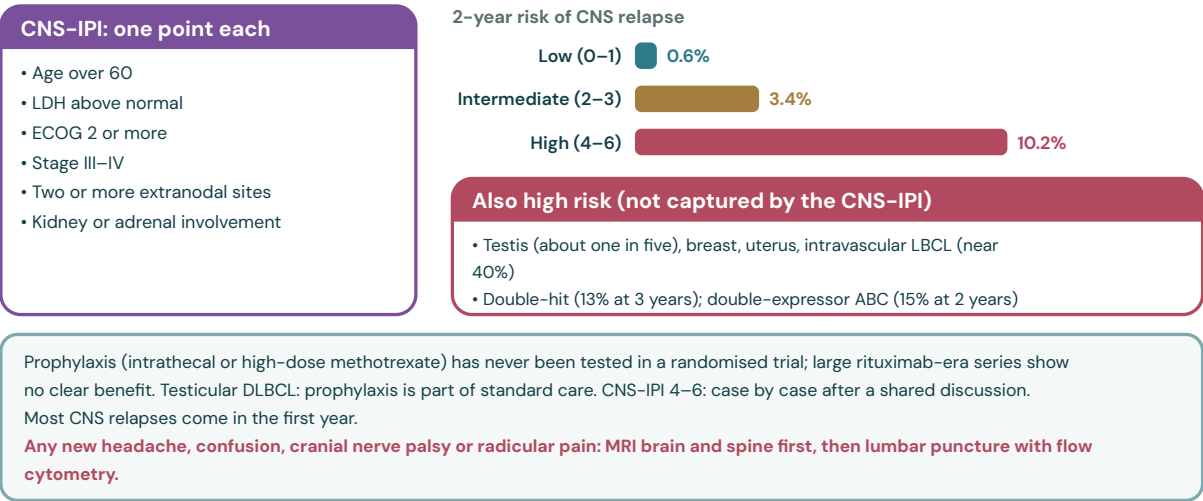


Figure 7. CNS relapse risk (Schmitz 2016; UpToDate secondary CNS lymphoma and advanced-stage DLBCL reviews; Lewis 2023 for high-dose methotrexate).

05 Local therapy: radiotherapy & surgery

Radiotherapy

- **Limited stage:** RT is now guided by PET. After three cycles of R-CHOP, Deauville 4 → ISRT 30–36 Gy with a boost to the avid site (or three more cycles); after six cycles for bulky disease (10 cm or more), Deauville 4 → ISRT 30 Gy. Conventional combined treatment (R-CHOP × 3 + ISRT) gives results similar to chemotherapy alone ([Lamy 2018^{\[19\]}](#)).
- **Testicular DLBCL:** scrotal RT (25–30 Gy) after R-CHOP prevents relapse in the other testis ([IELSG-10^{\[20\]}](#)).
- **Advanced stage:** no routine consolidation RT after a complete metabolic response (meta-analysis of 2414 patients: no survival gain, [Berger 2021^{\[21\]}](#)). Consider RT for isolated skeletal or paraspinal disease, or for an older patient with residual PET activity in a previously bulky mass.
- **Primary mediastinal lymphoma:** RT follows R-CHOP (combined modality) but can be left out after DA-EPOCH-R; after R-CHOP, a Deauville 1–2 PET predicts excellent control ([IELSG-26^{\[22\]}](#)). Weigh breast and heart dose in young women.
- **Primary CNS lymphoma:** whole-brain RT is now kept for patients who cannot have transplant or chemotherapy consolidation, because it impairs memory and thinking, especially after 60.
- **Primary cutaneous leg type:** ISRT after R-CHOP for limited disease.
- **Palliation:** frail patients, symptomatic masses, cord compression; bridging before CAR-T.

Surgery

- Surgery is for diagnosis (excision biopsy) and for complications such as bowel perforation, obstruction or bleeding. There is no role for debulking.
- If a surgeon finds a localised bowel lymphoma (often Burkitt in a child) and can remove it completely, that is appropriate; otherwise take tissue and stop.

SHARE WITH PATIENTS: SURGERY AND RADIOTHERAPY

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

[Every lymphoma needs surgery to remove the affected lymph nodes?](#)

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

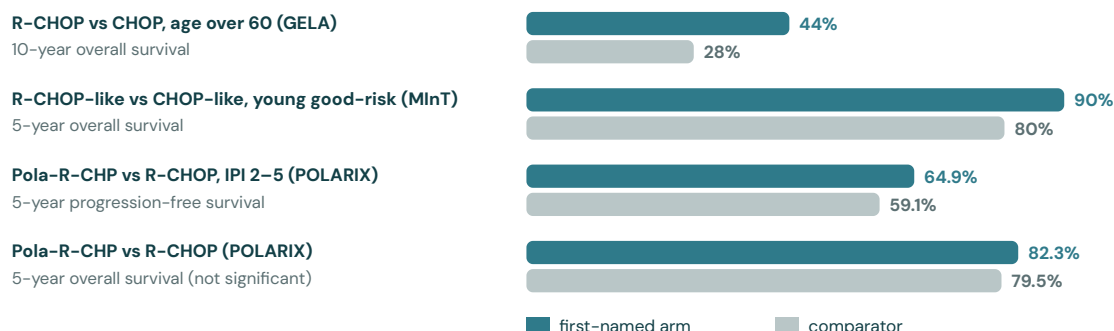
o6 Systemic therapy: indications & options

Limited-stage DLBCL (stage I–II)

- **PET-guided treatment is preferred**, split by bulk (a nodal mass of 10 cm or more). Always rituximab with the chemotherapy.
- **No bulk**: R-CHOP × 3, then PET3. Deauville 1–3 (about 89% in S1001) → one more cycle, four in total: 5-year OS 89% and PFS 87% ([S1001](#)^[23]). Deauville 4 → three more cycles or ISRT; Deauville 5 or extensive 4 → biopsy.
- **Why four cycles are enough**: in 592 patients aged 60 or under with no risk factors, four cycles of R-CHOP (plus two of rituximab alone) matched six for survival with less toxicity, and both treatment deaths were in the six-cycle arm ([FLYER](#)^[24]). UpToDate applies this to all ages.
- **Bulky disease**: R-CHOP × 6, then PET6: Deauville 1–3 → stop; 4 → ISRT 30 Gy; 5 → biopsy. If PET is not available: R-CHOP × 6 then RT.
- **Without PET guidance**: R-CHOP × 6, or R-CHOP × 3 + ISRT. Some experts use Pola-R-CHP when the IPI is 2 or more.
- **Primary testicular DLBCL** (the commonest testicular cancer over 60): orchiectomy, R-CHOP × 6, CNS prophylaxis and scrotal RT; orchiectomy alone is never enough, even in stage I ([IELSG-10](#)^[20]).

Advanced-stage DLBCL (stage III–IV)

First-line DLBCL: rituximab made the difference; polatuzumab adds a little



Six 21-day cycles, full doses (dose cuts lower cure). R-CHOP-14 and DA-EPOCH-R were not better and were more toxic. Interim PET does not guide escalation (PETAL). No consolidation transplant or maintenance in complete response.
POLARIX benefit was in non-GCB disease; grade ≥2 neuropathy 14–17% with either regimen.

Figure 8. First-line evidence (Coiffier 2010; Pfreundschuh 2006; POLARIX five-year report, Morschhauser 2025), as quoted in the UpToDate advanced-stage review. Compare arms within a trial, not across trials.

- **Always add rituximab**: in older adults it raised 10-year overall survival from 28% to 44% ([GELA](#)^[25], [E4494](#)^[26]); in younger good-risk patients 5-year survival rose from 80% to 90% ([MInT](#)^[27]).
- **R-CHOP or Pola-R-CHP, six 21-day cycles**. In 879 patients with IPI 2–5, Pola-R-CHP gave better 5-year progression-free survival (64.9% vs 59.1%); overall survival 82.3% vs 79.5% was not significantly different; the benefit was confined to non-GCB disease ([POLARIX](#)^[28]; [five-year update](#)^[3]). Cost and availability decide in many Indian centres.

- **Six cycles, not eight** ([RICOVER-60](#)^[29]); **21 days, not 14** ([UK trial](#)^[30], [LNHO3-6B](#)^[31]); **R-CHOP, not DA-EPOCH-R**, for DLBCL, NOS ([CALGB 50303](#)^[32]: more toxicity, no gain).
- **Full doses on time**: delivering less than about three-quarters of the planned doxorubicin early on lowers survival. G-CSF for patients aged 65 or more.
- **Interim PET** is optional; escalating treatment for a positive interim PET did not help ([PETAL](#)^[33]). Deauville 4 at interim: complete six cycles; progression: biopsy and treat as refractory.
- **After a complete response**: observation. Autologous transplant, rituximab or lenalidomide maintenance ([REMARC](#)^[34]) do not improve survival.

Older or frail adults and heart disease

- **Over 80** with adequate organ function: R-mini-CHOP × 6 ([Peyrade 2011](#)^[35]: 2-year OS 59%, PFS 47%; treatment-related deaths 8%). A steroid pre-phase improves fitness and lowers first-cycle toxicity.
- **Age alone is not a reason to withhold R-CHOP**: among patients over 80 in SEER, R-CHOP was the only treatment linked to better survival. Use a geriatric assessment.
- **LVEF below 40%**: replace doxorubicin with etoposide (R-CEOP, [Moccia 2021](#)^[36]) or gemcitabine (R-GCVP, [Fields 2014](#)^[37]). Milder dysfunction: liposomal or infusional doxorubicin, dexrazoxane, serial echo.
- **Unfit for any anthracycline**: chemotherapy-free mosunetuzumab-polatuzumab is under study (high response, but 12% fatal infections in a phase 2 study); palliation with steroids, rituximab or a single agent.

CNS prophylaxis

- No randomised trial supports routine prophylaxis; a meta-analysis and a 2418-patient series found no clear benefit from intrathecal or high-dose methotrexate ([Lewis 2023](#)^[38]).
- Testicular DLBCL: prophylaxis is part of standard treatment (about one in five relapse in the CNS, sometimes years later). CNS-IPI 4–6: some experts offer it case by case after a shared discussion ([Schmitz 2016](#)^[39]).

High-grade B-cell lymphoma with MYC and BCL2 rearrangements

- Worse outcomes with R-CHOP. No randomised trial defines the best regimen: many centres use DA-EPOCH-R; Pola-R-CHP trials included some of these patients. Check the CNS; offer a trial.
- MYC rearrangement alone, or a double-expressor without rearrangements, is treated as DLBCL, NOS.

Primary mediastinal large B-cell lymphoma

- Adults in their twenties and thirties, more often women: a locally invasive anterior mediastinal mass with SVC obstruction, effusions, cough or hoarseness. Cells are CD20+, often weakly CD30+ and PD-L1+, without CD10 or surface immunoglobulin; biology is closer to classic Hodgkin lymphoma.
- **Get enough tissue**: a surgical biopsy (mediastinoscopy or anterior mediastinotomy) is preferred; needle cores often crush the cells. Check the airway before anaesthesia.
- **Two acceptable first-line options**: R-CHOP × 6 followed by RT, or DA-EPOCH-R × 6–8 without RT ([Dunleavy 2013](#)^[40]). Choose by the RT field: avoid breast irradiation in young women when possible. A residual mass is common and often fibrosis: PET decides.

- **Relapse:** primary refractory or early relapse → CD19 CAR-T; later relapse → salvage and autologous transplant, or immunotherapy. PD-1 blockade works in PMBL ([pembrolizumab](#)^[41]; [nivolumab with brentuximab vedotin](#)^[42]).

Burkitt lymphoma

Burkitt lymphoma: the fastest-growing human cancer, and highly curable

Endemic

- Equatorial Africa; children
- Jaw or facial bone tumour
- EBV in nearly every case

Sporadic

- Children and young men worldwide
- Abdominal mass; mimics appendicitis or intussusception
- 30% of childhood NHL, under 1% of adult NHL

Immunodeficiency

- HIV, transplant
- Nodes more often involved
- Same treatment as sporadic

The pathologist's clues

- Monomorphic medium cells, "starry sky"
- Ki-67 close to 100%
- CD10+, BCL2-, TdT-; surface IgM
- t(8;14) or t(2;8), t(8;22): MYC + Ig

BL-IPI: age ≥40, ECOG ≥2, LDH >3× ULN, CNS disease (3-year OS)



Rituximab added: 3-year EFS 75% vs 62%, OS 83% vs 70%

Start promptly: rasburicase and hydration for tumour lysis, lumbar puncture, HIV test. Fit: R-CODOX-M/R-IVAC with CNS prophylaxis.

Older or less fit: DA-EPOCH-R with intrathecal methotrexate. Never treat Burkitt with R-CHOP alone. Relapse is rarely salvaged.

Figure 9. Burkitt lymphoma (UpToDate Burkitt diagnosis and adult treatment reviews; Olszewski 2021 for the BL-IPI; Ribrag 2016 for rituximab).

- **Start promptly,** after tumour lysis prophylaxis (hydration, rasburicase), lumbar puncture, marrow and HIV test. Avoid dose cuts.
- **Fit adults:** short intensive regimens with CNS prophylaxis, such as R-CODOX-M/R-IVAC (Magrath); rituximab usually from cycle 2 to limit lysis. Rituximab raised 3-year EFS from 62% to 75% ([Ribrag 2016](#)^[43]); in a large German series 5-year OS was 80%, but 62% over age 55 ([Hoelzer 2014](#)^[44]).
- **Older or less fit:** DA-EPOCH-R with intrathecal methotrexate ([Roschewski 2020](#)^[45]). A randomised comparison closed early: similar 2-year PFS, fewer infections with DA-EPOCH-R ([HOVON/SAKK](#)^[46]).
- **Prognosis:** BL-IPI ([Olszewski 2021](#)^[47]). Relapse after adequate treatment is rarely salvaged; CAR-T results are disappointing.
- **Children:** paediatric protocols with rituximab; adding rituximab raised 3-year OS from 87.3% to 95.1% in high-risk mature B-cell lymphoma ([Inter-B-NHL](#)^[48]). Older adolescents may receive paediatric or adult regimens.

Primary CNS lymphoma

- **Brain, eyes, meninges or spinal cord only.** Stereotactic biopsy before steroids; eye examination, CSF and body PET. Age and performance status predict survival most strongly.
- **Induction:** a high-dose methotrexate-based combination with rituximab (MTR or R-MPV for most; MATRix for younger fit adults, [IELSG32](#)^[49]); MRI every two to four methotrexate doses, aiming for a complete response. Kidney function and fitness, not age over 65 alone, decide eligibility.

- **Consolidation:** fit responders → thiotepa-based high-dose chemotherapy and autologous transplant ([PRECIS](#) ^[50]; [MATRix/IELSG43](#) ^[51]); others → cytarabine-based chemotherapy, whole-brain RT or observation.
- **Relapse:** methotrexate again after a long remission, transplant in selected patients, CAR-T, ibrutinib or lenalidomide, RT or a trial.

CNS involvement by systemic DLBCL (secondary CNS lymphoma)

- **Steroids and antiseizure drugs first** to restore function; prognosis is poor overall, but younger fit patients with synchronous disease or an isolated CNS relapse can be cured.
- **CNS and systemic disease at diagnosis:** high-dose methotrexate with R-CHOP or Pola-R-CHP, or MATRix-RICE ([MARIETTA](#) ^[52]), then autologous transplant in responders.
- **CNS relapse after R-CHOP:** CAR-T for most; otherwise a methotrexate-based regimen then transplant. Intrathecal therapy only when systemic methotrexate is not possible, or briefly for very symptomatic leptomeningeal disease.

Special settings

Same disease, different patient: how the plan changes

Over 80, or frail • Geriatric assessment (ADL, IADL, comorbidity) • Steroid pre-phase; G-CSF • R-mini-CHOP × 6: 2-year OS 59%	Weak heart (LVEF <40%) • R-CEOP or R-GCVP instead of doxorubicin • Milder: liposomal or infusional doxorubicin, dexrazoxane • Cardio-oncology input	People living with HIV • Continue ART; check interactions • Rituximab if CD4 ≥50 • R-CHOP or DA-EPOCH-R; co-trimoxazole
Richter transformation (CLL) • Biopsy the most PET-avid node • R-CHOP ± venetoclax; trial if on a BTK inhibitor • Allogeneic transplant in first remission	After a transplant (PTLD) • Reduce immunosuppression first • Rituximab, then R-CHOP if no complete response • EBV-specific T cells where available	Primary cutaneous, leg type • PET must show skin-only disease • R-CHOP; add ISRT for limited disease • More than half relapse

Figure 10. Special settings, from the UpToDate advanced-stage, older-adult, HIV, Richter, PTLD and cutaneous leg-type reviews (Peyrade 2011; Moccia 2021; Fields 2014; Davids 2022; Trappe 2012 and 2017).

- **People living with HIV:** outcomes now match those without HIV. Continue antiretroviral therapy (check interactions with an HIV pharmacist), give co-trimoxazole, add rituximab when CD4 is 50 or more; R-CHOP or DA-EPOCH-R ([Barta 2013](#) ^[53]). Plasmablastic and primary effusion lymphoma: EPOCH or CHOP.
- **Richter transformation:** biopsy the most PET-avid node; R-CHOP with venetoclax for most ([Davids 2022](#) ^[54]); clinical trial if it arose on a BTK inhibitor; allogeneic transplant in first remission for fit patients (unless clonally unrelated).
- **PTLD:** reduce immunosuppression first; rituximab, then R-CHOP if the response is incomplete ([PTLD-1](#) ^[55]; [Trappe 2017](#) ^[56]); EBV-specific T cells where available.
- **Primary cutaneous DLBCL, leg type:** R-CHOP, plus ISRT for limited disease; more than half relapse ([Grange 2007](#) ^[57]).

Relapsed or refractory large B-cell lymphoma

Relapsed or refractory large B-cell lymphoma: timing and fitness decide

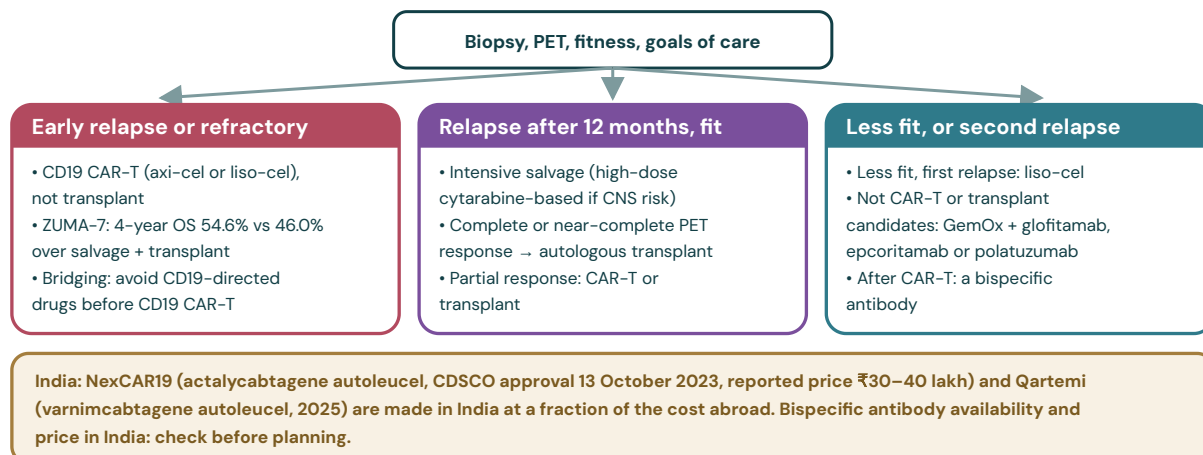


Figure 11. Relapsed or refractory disease (UpToDate reviews of first relapse in fit patients and of second relapse or unfit patients; ZUMA-7 overall survival, Westin 2023; STARGLO, Abramson 2024). Indian products web-verified 16 October 2026.

- **Biopsy the first relapse** (it may be another lymphoma, infection or a second cancer) and re-check CD19 before CAR-T. Refractory disease does badly with chemotherapy ([SCHOLAR-1](#)^[58]). Assess fitness by performance status and comorbidity, not age alone.
- **Refractory or relapse within 12 months, fit:** CD19 CAR-T with axi-cel or liso-cel rather than transplant. Axi-cel improved 4-year overall survival to 54.6% from 46.0% ([ZUMA-7](#)^[59]; [Westin 2023](#)^[4]); liso-cel improved event-free survival ([TRANSFORM](#)^[60]); tisa-cel did not ([BELINDA](#)^[61]). If bridging is needed, avoid CD19-directed drugs before CD19 CAR-T.
- **First relapse after 12 months, fit:** intensive salvage (high-dose cytarabine-based if the CNS is involved or at risk), then high-dose therapy and autologous transplant for a complete or near-complete PET response ([CORAL](#)^[62]); partial response → CAR-T or transplant. No rituximab maintenance afterwards.
- **Less fit but not frail:** liso-cel for a first relapse. **Second or later relapse:** CAR-T if not given before ([TRANSCEND](#)^[63]); after CAR-T, a bispecific antibody ([glofitamab](#)^[64], [epcoritamab](#)^[65]).
- **Not a candidate for transplant or CAR-T:** GemOx with glofitamab (median OS 25.5 vs 12.9 months over R-GemOx, complete responses 58.5% vs 25.3%, [STARGLO](#)^[66]), epcoritamab or polatuzumab. Other options: Pola-BR ([Sehn 2020](#)^[67]), tafasitamab-lenalidomide ([L-MIND](#)^[68]), loncastuximab ([LOTIS-2](#)^[69]). Frail patients: palliation and supportive care.

CAR-T and bispecific antibodies: the two toxicities to recognise early

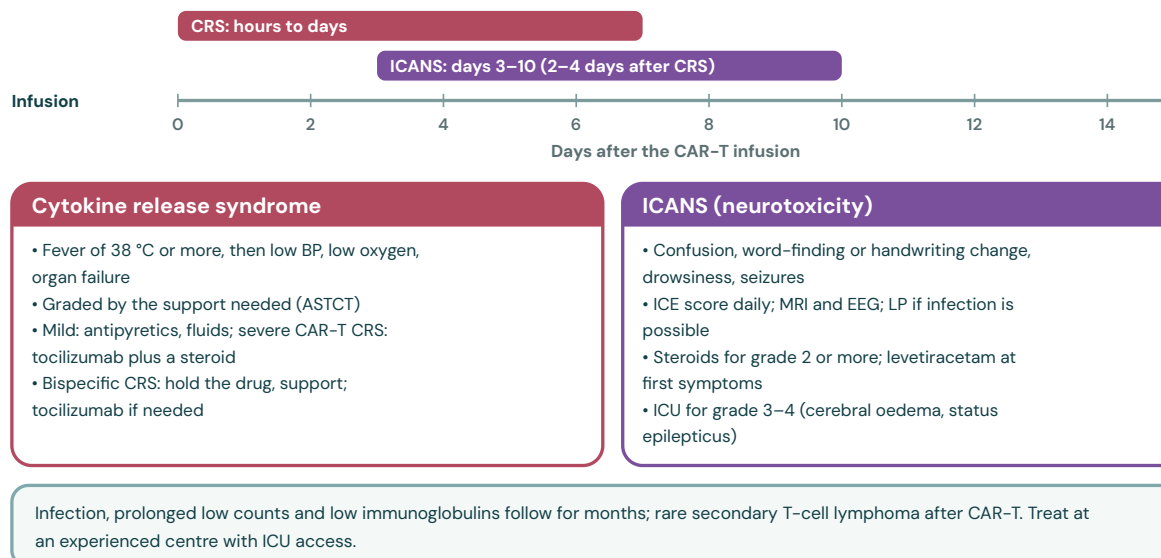


Figure 12. CAR-T and bispecific toxicity (UpToDate reviews of cytokine release syndrome and of ICANS). Illustrative timeline; onset differs by product.

- **CRS:** fever of 38 °C or more within hours to days, then low blood pressure, hypoxia and organ failure; graded by the support needed. Severe CAR-T CRS: tocilizumab plus a steroid. Bispecific CRS: hold the drug and support; tocilizumab if needed. Infection is the main mimic.
- **ICANS:** 3–10 days after CAR-T, usually 2–4 days after CRS begins: confusion, word-finding and handwriting change, seizures, rarely cerebral oedema. Daily ICE score; steroids for grade 2 or more; levetiracetam at the first neurological symptom; ICU for grade 3–4.

Supportive care that prevents deaths

- **Tumour lysis:** risk by entity, bulk, LDH, uric acid and kidney function. High risk (Burkitt, bulky high-LDH DLBCL): IV fluids plus rasburicase (not in G6PD deficiency); intermediate: fluids plus allopurinol. Most lysis occurs 12–72 hours after starting ([Coiffier 2008^{\[70\]}](#)).
- **Hepatitis B:** test HBsAg and anti-HBc before rituximab (anti-HBs does not remove the risk). HBsAg-positive with rituximab: very high risk (over 20%); anti-HBc-positive, HBsAg-negative: moderate risk (1–10%; 8% with anti-HBs vs 23% without in one lymphoma study). Both get tenofovir or entecavir, not lamivudine, starting before rituximab and continuing at least 12 months after the last dose ([Huang 2014^{\[71\]}](#); [ASCO 2020^{\[72\]}](#)).
- **Infection:** G-CSF for age 65 or more and for intensive regimens; co-trimoxazole for HIV and dose-dense or intensive regimens; vaccines before treatment, no live vaccines during it.

SHARE WITH PATIENTS: TREATMENT, IMMUNOTHERAPY AND RELAPSE

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

[Aggressive lymphoma is always harder to cure than slow-growing lymphoma?](#)

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

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

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

If lymphoma returns after chemotherapy, no effective treatment remains?

CAR-T cell therapy can cure every lymphoma?

India now (October 2026)

- Rituximab biosimilars made in India are widely used and have made R-CHOP the routine first-line standard; screen for hepatitis B before every rituximab course.
- Polatuzumab vedotin (Polivy, Roche) was approved by the DCGI with R-CHP for untreated DLBCL in September 2023 (Roche India). Its cost limits use; reserve it for non-GCB, IPI 2–5 disease when the patient can afford six cycles.
- CAR-T: NexCAR19 (actalycabtagene autoleucel; ImmunoACT with IIT Bombay and Tata Memorial) received CDSCO approval on 13 October 2023 for relapsed or refractory B-cell lymphoma and leukaemia, at a reported ₹30–40 lakh, about a tenth of the price abroad ([pivotal trial](#)^[73]); Qartemi (varnimcabtagene autoleucel, Immuneel) followed in January 2025. Hospital costs come on top.
- Bispecific antibodies (glofitamab, epcoritamab) and liso-cel or axi-cel: availability and price in India not verified; check before planning.
- G6PD deficiency is not rare in India: test before rasburicase where possible. When PET-CT is not available, contrast CT staging and response assessment are acceptable.

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 biopsy (several cores if not feasible)	Every suspected case, urgently, before steroids	Diagnosis and entity	FNA cannot diagnose or exclude lymphoma; avoid inguinal nodes; steroids blur the picture
IHC: CD20, CD10, BCL6, MUM1, Ki-67, MYC, BCL2, CD5, CD30; EBER	Every biopsy	Cell of origin (Hans); double-expressor; EBV-positive DLBCL; mimics	IHC agrees with gene-expression profiling in about 80%
FISH for MYC (then BCL2, BCL6)	All large B-cell lymphomas, at least when MYC protein is high	High-grade B-cell lymphoma with MYC and BCL2 rearrangements; Burkitt	MYC IHC can be falsely low; MYC partner gene matters
PET-CT	Staging and end of treatment (4–8 weeks after chemotherapy)	Lugano stage, marrow and extranodal disease; complete metabolic response	Interim PET does not guide escalation; inflammation and infection take up FDG
CBC, chemistry, uric acid, LDH, calcium	Baseline and before cycle 1	IPI; tumour lysis risk	High LDH or uric acid: start lysis prophylaxis before treatment
HBsAg, anti-HBc (HBV DNA if either positive), HCV, HIV	Before rituximab	Antiviral prophylaxis; HIV changes regimen choice and supportive care	Anti-HBc alone still carries reactivation risk with rituximab
Echocardiogram or MUGA	Before anthracycline	LVEF below 40%: replace doxorubicin	Baseline for survivorship

Test	When	What it changes	Pitfalls
CNS-IPI; MRI and lumbar puncture with flow cytometry if risk or symptoms	Baseline	CNS-directed therapy; Burkitt and HIV-Burkitt always have an LP	Cytology misses cases that flow cytometry finds
Bone marrow biopsy	Optional if PET shows marrow disease; consider for cytopenias	Stage; discordant small-cell involvement	PET may miss diffuse low-volume marrow disease
Pregnancy test; fertility counselling; sperm banking	Before treatment	Timing and options	Fertility is usually preserved after R-CHOP; transplant and repeated lines lower it

Table B. Treatment by setting and entity

Setting	Standard choice	Key evidence	Notes
DLBCL stage I–II, no bulk (under 10 cm)	R-CHOP × 3 → PET3: Deauville 1–3 → one more cycle (4 in total)	S1001 ^[23] , FLYER ^[24]	Deauville 4 → 3 more cycles or ISRT; 5 → biopsy. Alternatives: R-CHOP × 6, or × 3 + ISRT
DLBCL stage I–II, bulky (10 cm or more)	R-CHOP × 6 → PET6: Deauville 4 → ISRT 30 Gy	UNFOLDER, RICOVER-noRTH (no routine RT)	Some use Pola-R-CHP for IPI ≥2
Primary testicular DLBCL	Orchiectomy + R-CHOP × 6 + CNS prophylaxis + scrotal RT	IELSG-10 ^[20]	Orchiectomy alone is never enough
DLBCL stage III–IV	R-CHOP × 6 or Pola-R-CHP × 6	POLARIX ^[28] , RICOVER-60 ^[29] , MinT ^[2]	Pola-R-CHP favoured for non-GCB and IPI 2–5 when affordable
Age over 80 or frail	R-mini-CHOP × 6 after a steroid pre-phase	Peyrade 2011 ^[35]	Geriatric assessment; G-CSF
LVEF below 40%	R-CEOP or R-GCVP	Moccia 2021 ^[36] , Fields 2014 ^[37]	Cardio-oncology input
HGBL with MYC and BCL2 rearrangements	No randomised standard: DA-EPOCH-R or Pola-R-CHP commonly used; trial preferred	Retrospective series	High CNS risk; consider CNS-directed therapy
Primary mediastinal LBCL	R-CHOP × 6 + RT, or DA-EPOCH-R × 6–8 without RT	Dunleavy 2013 ^[40] , IELSG-26 ^[22]	Avoid RT to breast tissue in young women where possible
Burkitt lymphoma	R-CODOX-M/R-IVAC (fit); DA-EPOCH-R (older or less fit)	Ribrag 2016 ^[43] , HOVON/SAKK ^[46]	Rituximab from cycle 2; CNS prophylaxis always
Primary CNS lymphoma	High-dose methotrexate combination + rituximab → autologous transplant if fit	IELSG32 ^[49] , PRECIS ^[50]	Kidney function and fitness, not age, decide
Synchronous systemic + CNS DLBCL	High-dose methotrexate with R-CHOP or Pola-R-CHP, or MATRix-RICE	MARIETTA ^[52]	Transplant consolidation in responders
Relapse within 12 months or refractory, fit	CD19 CAR-T: axi-cel or liso-cel	ZUMA-7 ^[4] , TRANSFORM ^[60] , not tisa-cel (BELINDA ^[61])	India: NexCAR19, Qartemi
Later first relapse, fit	Intensive salvage → autologous transplant if complete or near-complete response	CORAL ^[62]	No rituximab maintenance after transplant

Setting	Standard choice	Key evidence	Notes
Second relapse, or not fit for transplant/CAR-T	GemOx + glofitamab, epcoritamab or polatuzumab; bispecific after CAR-T	STARGLO^[66] , EPCORE^[65]	Others: Pola-BR, tafasitamab–lenalidomide, loncastuximab; frail: palliation

Table C. Regimens and drugs: evidence and best fit

Regimen or drug	Best fit	Evidence	Main toxicity
R-CHOP (21-day)	Default first line for most DLBCL	Cures about 60% of advanced disease; 10-year OS 44% vs 28% over CHOP in older adults	Neutropenia, neuropathy, cardiomyopathy, hyperglycaemia
Pola-R-CHP	IPI 2–5, especially non-GCB	POLARIX: 5-year PFS 64.9% vs 59.1%; OS difference not significant	Similar to R-CHOP; neuropathy 14–17% grade ≥2
R-mini-CHOP	Over 80, or frail	2-year OS 59%, PFS 47%	Febrile neutropenia 7%; treatment-related death 8%
DA-EPOCH-R	PMBL; Burkitt in older or less fit; HIV-DLBCL; double-hit (debated)	No better than R-CHOP in DLBCL (CALGB 50303); excellent PMBL series	More neutropenia, mucositis, neuropathy; needs infusion pump or admission
R-CODOX-M/R-IVAC	Fit adults with Burkitt	Rituximab: 3-year EFS 75% vs 62%; OS 83% vs 70%	Severe myelosuppression, mucositis; prolonged admission
CD19 CAR-T	Early relapse or refractory; third line	ZUMA-7: 4-year OS 54.6% vs 46.0%	Cytokine release syndrome, ICANS, prolonged cytopenias, infections
Bispecific antibodies (glofitamab, epcoritamab)	Transplant-ineligible relapse; after CAR-T	STARGLO: median OS 25.5 vs 12.9 months with GemOx	Cytokine release syndrome (step-up dosing), infections
Rituximab (any combination)	Every CD20-positive aggressive lymphoma	Survival gain in DLBCL, Burkitt and children	Infusion reactions, HBV reactivation, PML (rare), low immunoglobulins

Table D. Managing problems during treatment

Problem	Prevent	Recognise	Act
Tumour lysis	High risk (Burkitt, bulky, high LDH or uric acid, kidney impairment): IV fluids + rasburicase; intermediate: fluids + allopurinol	K, phosphate, uric acid up; calcium down; creatinine rising; arrhythmia	Monitor closely for the first 72 hours; kidney team; check G6PD before rasburicase where possible
Hepatitis B reactivation	Screen HBsAg and anti-HBc; tenofovir or entecavir from before rituximab until at least 12 months after the last dose	Rising ALT, HBV DNA	Hold rituximab; hepatology; entecavir or tenofovir rather than lamivudine
Febrile neutropenia	G-CSF for age 65+ on curative chemotherapy, and for R-CHOP-14 or intensive regimens	Fever 38 °C or more	Same-day assessment; empirical antibiotics within an hour
Infections	Co-trimoxazole for HIV, R-CHOP-14 and intensive regimens; aciclovir as indicated	Cough, breathlessness (PJP), shingles	Low immunoglobulins with repeated infections: replace

Problem	Prevent	Recognise	Act
Cardiotoxicity	Baseline echo; control risk factors; dexrazoxane or liposomal doxorubicin in selected patients	Breathlessness, oedema, falling LVEF	Cardio-oncology; switch regimen if LVEF below 40%
Neuropathy (vincristine, polatuzumab)	Ask at every cycle	Numb or weak hands and feet, constipation	Reduce or omit vincristine; never omit the curative backbone casually
CAR-T and bispecific toxicity	Step-up dosing for bispecifics; experienced centre with ICU	Fever ≥ 38 °C, low BP, hypoxia (CRS); confusion, word-finding or writing change (ICANS)	Severe CRS: tocilizumab + steroid; ICANS grade ≥ 2 : steroids, levetiracetam

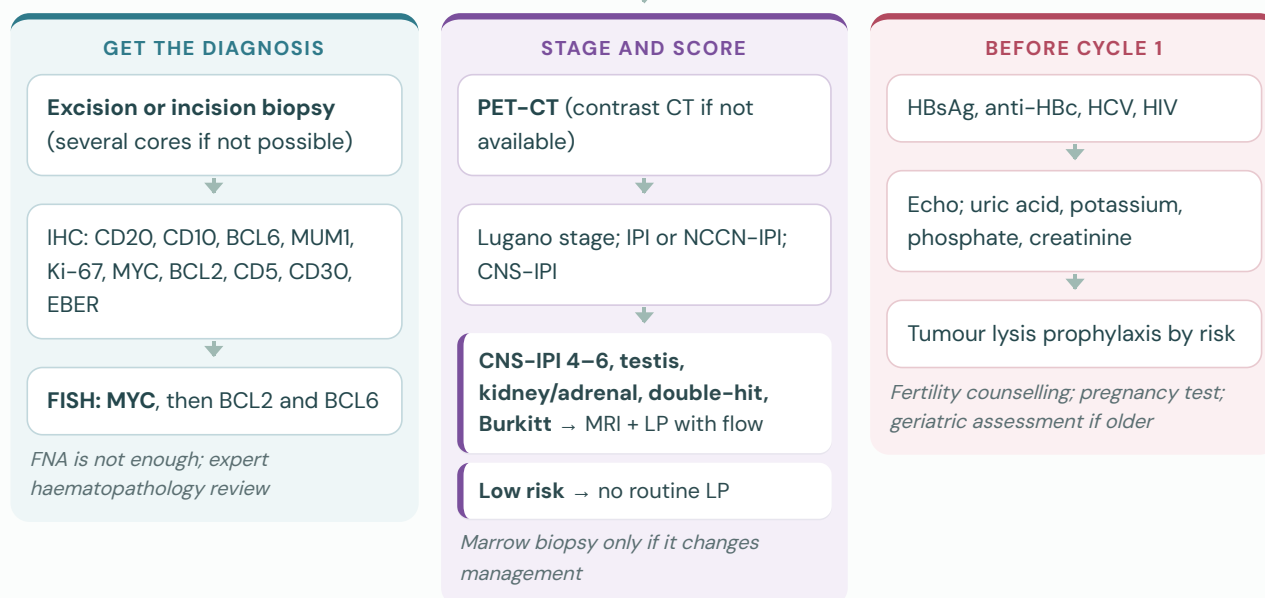
07 Management algorithms

These decision paths pull together sections 02–06. Colours: teal for standard paths, purple for intermediate or special settings, rose for high-risk or relapse paths.

ALGORITHM 1

Suspected aggressive B-cell lymphoma: from a mass to a diagnosis and a plan

Rapidly growing node or mass, B symptoms or a high LDH → urgent biopsy before steroids → treat emergencies (SVC, cord, airway, lysis) in parallel



All patients: discuss in a lymphoma multidisciplinary team · start within days · steroid pre-phase for frail or very symptomatic patients · vaccines before treatment.

ALGORITHM 2

DLBCL first line by stage and fitness

DLBCL, NOS (MYC/BCL2 double-hit excluded) → stage, bulk, IPI, age, heart, fitness

LIMITED STAGE (I–II)

No bulk → R-CHOP × 3 → PET3

Bulky ≥10 cm → R-CHOP × 6 → PET6

PET3 Deauville 1–3 → one more cycle (4 in total); 4 → 3 more or ISRT

PET6 Deauville 4 → ISRT 30 Gy; 5 → biopsy

Testis: orchiectomy + R-CHOP × 6 + CNS prophylaxis + scrotal RT

ADVANCED STAGE (III–IV)

R-CHOP × 6 or Pola-R-CHP × 6 (non-GCB, IPI 2–5)

Full doses on time; G-CSF from age 65

End-of-treatment PET 4–8 weeks later

No interim-PET escalation; no maintenance or consolidation transplant

OLDER, FRAIL OR HEART DISEASE

Over 80 → steroid pre-phase, R-mini-CHOP × 6

LVEF below 40% → R-CEOP or R-GCVP

Frail → steroid ± rituximab, single agent, palliative RT

Geriatric assessment, not age alone

All patients: CNS prophylaxis for testicular disease, case by case for CNS-IPI 4–6 · Deauville 4–5 at the end → biopsy before calling it refractory · RT for selected residual or skeletal sites.

ALGORITHM 3

Special entities and settings

Pathology or history points away from DLBCL, NOS → treat the entity, not only the stage

HIGHLY AGGRESSIVE

Burkitt: fit → R-CODOX-M/R-IVAC; older → DA-EPOCH-R; CNS prophylaxis

HGBL MYC + BCL2: DA-EPOCH-R or Pola-R-CHP; trial; CNS work-up

Systemic + CNS: high-dose methotrexate with R-CHOP, or MATRix-RICE

Rasburicase and hydration first; start promptly

SITE-DEFINED

Primary mediastinal: R-CHOP × 6 + RT, or DA-EPOCH-R without RT

Primary CNS: methotrexate combination + rituximab → transplant if fit

Cutaneous leg type: R-CHOP ± ISRT

Surgical biopsy for PMBL; biopsy before steroids in PCNSL

HOST-DEFINED

HIV: continue ART; rituximab if CD4 ≥50; R-CHOP or DA-EPOCH-R

PTLD: reduce immunosuppression → rituximab → R-CHOP

Richter: R-CHOP ± venetoclax → allogeneic transplant in CR

Children: paediatric protocols with rituximab

All: expert haematopathology · HIV test for every aggressive lymphoma · fertility counselling before intensive regimens.

ALGORITHM 4

Relapsed or refractory large B-cell lymphoma

New mass, rising LDH or a Deauville 4–5 residue → biopsy (exclude infection, inflammation, a second cancer; check CD19) → PET, fitness

REFRACTORY OR RELAPSE <12 MONTHS, FIT

CD19 CAR-T: axi-cel or liso-cel
(NexCAR19 or Qartemi in India)

Bridging if needed: no CD19-directed drugs

CAR-T not possible → GemOx + bispecific, or salvage

CR after CAR-T → watch

Refer early: making the cells takes weeks

FIRST RELAPSE ≥12 MONTHS, FIT

Intensive salvage (high-dose cytarabine-based if CNS risk)

CR or near-CR → high-dose therapy + autologous transplant

PR → CAR-T or transplant

Stable or progressive → treat as second relapse

LESS FIT, OR SECOND RELAPSE

Less fit, first relapse → liso-cel

No CAR-T or transplant → GemOx + glofitamab, epcoritamab or polatuzumab

After CAR-T → bispecific antibody

Frail: palliation, RT, steroids, supportive care

All: clinical trial where available · CRS and ICANS plan before CAR-T or bispecifics · infection prophylaxis and immunoglobulin replacement as needed · discuss cost and scheme cover early.

o8 Survivorship, follow-up & late effects

A simple follow-up rhythm after treatment of aggressive B-cell lymphoma

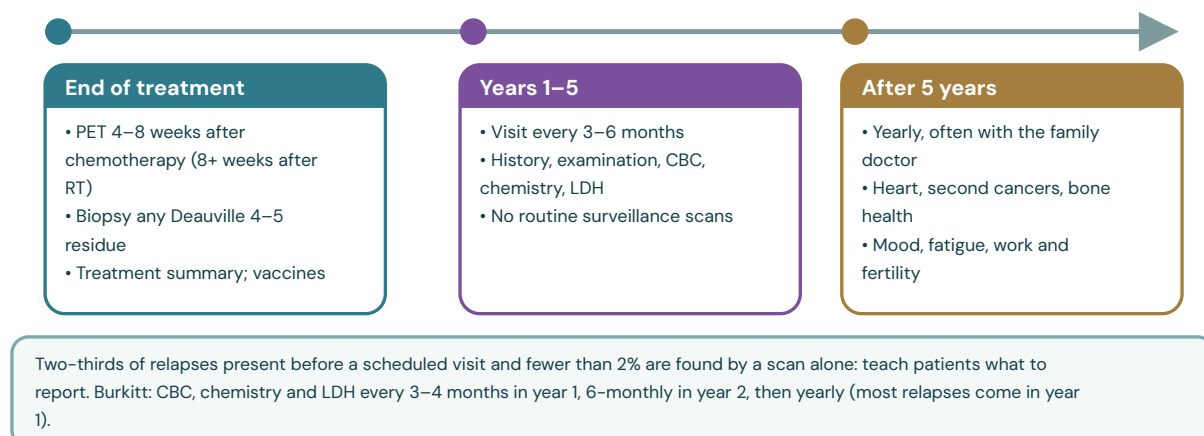


Figure 13. A simple follow-up rhythm, adapted from the UpToDate advanced-stage DLBCL, Burkitt treatment and NHL survivorship reviews. Individualise by age, entity and treatment received.

- **End-of-treatment PET** 4–8 weeks after chemotherapy (at least 8 weeks after RT). Deauville 1–3 = complete metabolic response; 4–5 → biopsy before calling it refractory.
- **Visits** every 3–6 months for 5 years (history, examination, CBC, chemistry, LDH), then yearly. **No routine surveillance scans** in complete response: fewer than 2% of relapses are found by a scan before symptoms, survival is the same, and scans add radiation and false alarms ([Thompson 2014](#)^[74], [El-Galaly 2015](#)^[75]).
- **Vaccines:** influenza and pneumococcal vaccines; no live vaccines for at least six months after rituximab; responses to vaccines are weak in the first months.

When relapses happen: mostly in the first two years

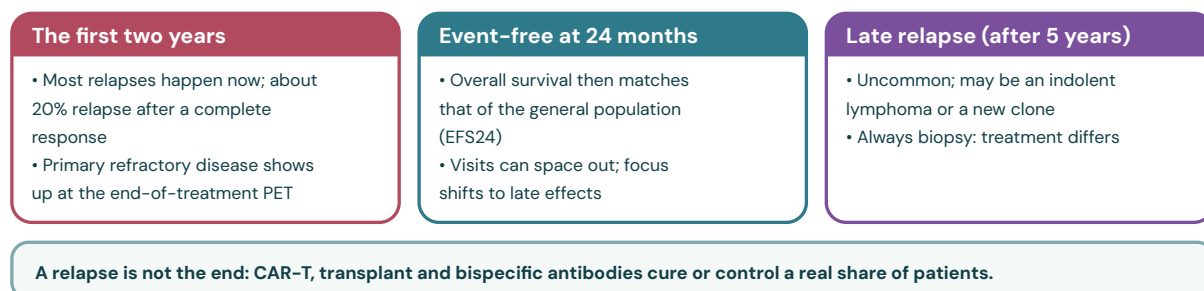


Figure 14. When relapses happen (Thompson 2014; Maurer 2014; Larouche 2010 as quoted in the UpToDate advanced-stage review).

Late effects after cure: what survivors carry**Heart**

- Heart failure 3.9× the population after DLBCL treatment
- Higher in women (5.3×) and if treated at 40 or younger (10.5×)
- Cardiovascular disease 12% at 5 and 22% at 10 years after doxorubicin regimens

Second cancers

- Leukaemia (AML) about 5× after DLBCL
- Solid tumours, especially in RT fields and in the young
- Risk persists for 25 years or more

Everyday life

- Fatigue in up to two in three; severe in 37% at 11 years
- Post-traumatic stress symptoms in 39%
- Fertility usually preserved after R-CHOP

Rare but serious: PML after rituximab (median 5.5 months after the last dose; mostly fatal). Hypothyroidism after neck RT: TSH yearly.

Control blood pressure, lipids, sugar and weight; stop smoking; exercise 150 minutes a week (better quality of life).

Figure 15. Late effects (Geurts 2026; Moser 2006; Morton 2010; Carson 2009; UpToDate survivorship review).

- **Heart:** baseline cardiology review after treatment, blood pressure, lipids, sugar, weight and smoking; echo if symptoms or after chest RT ([Geurts 2026](#)^[76]; [Moser 2006](#)^[77]).
- **Second cancers:** age-appropriate screening, yearly skin check, breast screening from 25 or 8 years after chest RT (whichever is later); report new symptoms ([Morton 2010](#)^[78]).
- **Mind and body:** ask about fatigue, mood, post-traumatic stress, work and money; encourage 150 minutes of exercise a week. Neurocognitive screening after CNS treatment.
- **PML:** new neurological symptoms after rituximab need an urgent MRI ([Carson 2009](#)^[79]).

SHARE WITH PATIENTS: LIFE AFTER LYMPHOMA

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?](#)

09 Landmark trials

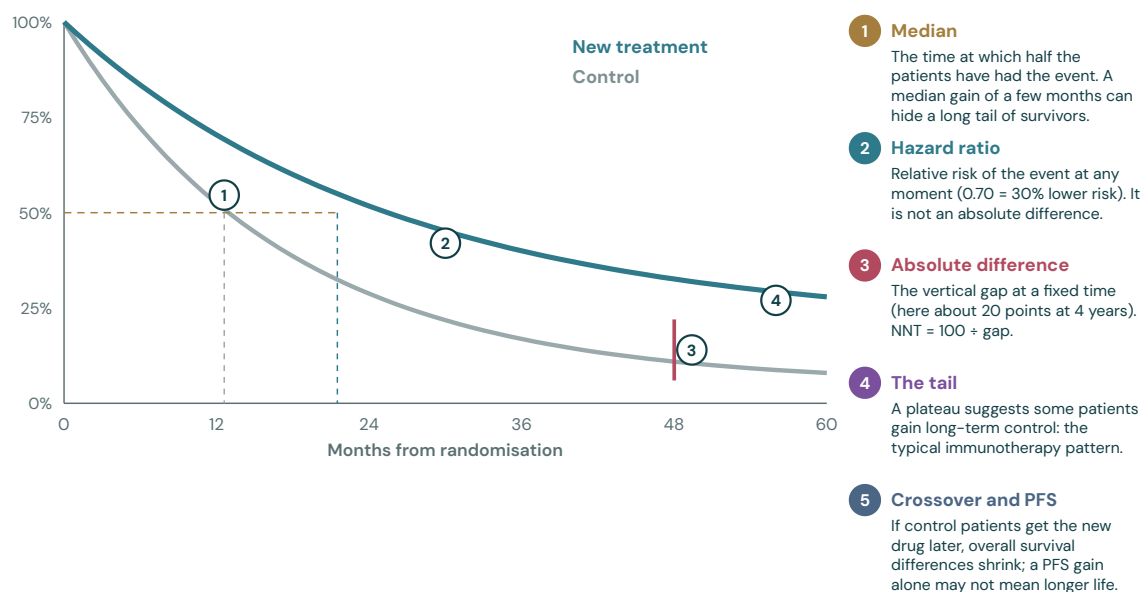
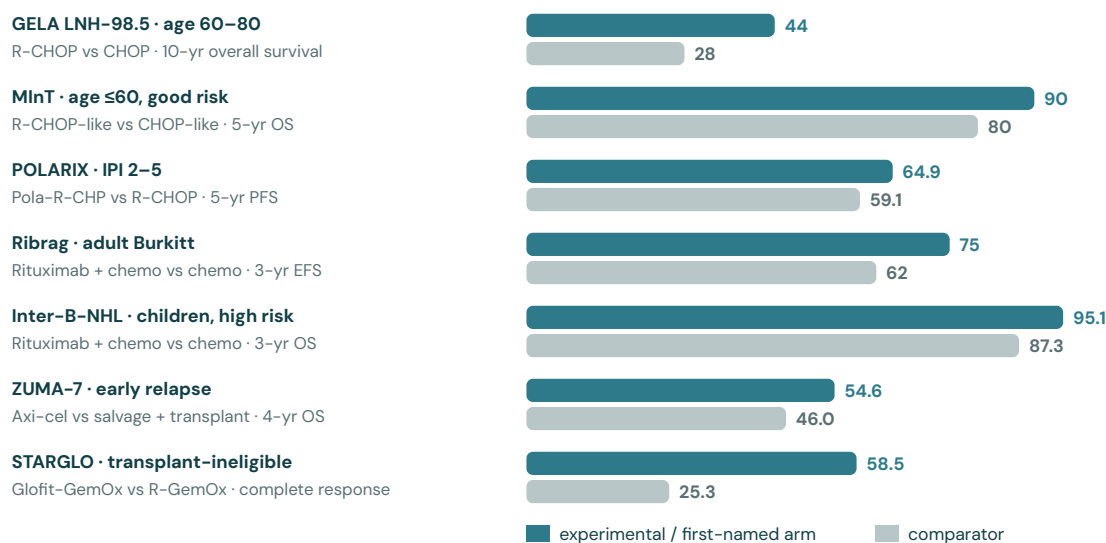


Figure 16. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

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



Endpoints and time points differ: compare arms within a trial, not across trials.

Figure 17. Landmark results. First-line and Burkitt trials as reported in the UpToDate reviews; ZUMA-7 and STARGLO web-verified (16 October 2026).

- [GELA LNH-98.5](#)^[25] and its [10-year update](#)^[1]: older adults → rituximab plus CHOP raised 10-year OS from 28% to 44% → R-CHOP standard.
- [MInT](#)^[2]: younger good-risk patients → rituximab improved 5-year OS from 80% to 90% → rituximab for all ages.
- [RICOVER-60](#)^[29]: six versus eight cycles of R-CHOP-14 → no difference → six cycles.
- [CALGB 50303](#)^[32]: DA-EPOCH-R vs R-CHOP → more toxicity, no gain → R-CHOP for DLBCL, NOS.

- **POLARIX**^[28]: Pola-R-CHP vs R-CHOP in IPI 2–5 → better PFS (5-year 64.9% vs 59.1%), similar OS → first change to first-line therapy in two decades.
- **PETAL**^[33]: escalation after a positive interim PET → no benefit → do not escalate on interim PET.
- **FLYER**^[24]: low-risk limited stage → four cycles as good as six → shorter treatment for the best-risk group.
- **ZUMA-7**^[59]: axi-cel vs salvage + transplant in early relapse → better EFS and 4-year OS (54.6% vs 46.0%) → CAR-T as second line.
- **STARGLO**^[66]: glofitamab-GemOx vs R-GemOx, transplant-ineligible → median OS 25.5 vs 12.9 months → first bispecific with a survival gain.
- **Ribrag 2016**^[43] and **Inter-B-NHL**^[48]: rituximab improves survival in Burkitt in adults and in children.

10 Practice pearls & pitfalls

- A node that keeps growing over a few weeks needs an excision biopsy, not more antibiotics, anti-TB tablets or steroids.
- FNA cannot diagnose or exclude lymphoma; architecture, IHC and FISH need a core or the whole node.
- Ask for *MYC* FISH on every large B-cell lymphoma: double-hit lymphoma looks like DLBCL under the microscope.
- Check HBsAg and anti-HBc before the first rituximab dose; anti-HBc alone still needs a plan.
- Score the IPI and the CNS-IPI on day one and write both in the notes.
- Burkitt lymphoma and bulky high-LDH disease: start lysis prophylaxis before the first dose; check G6PD before rasburicase.
- Six cycles of R-CHOP on time and at full dose cure more patients than any dose-reduced "gentle" plan; give G-CSF from age 65.
- Pola-R-CHP helps mostly in non-GCB disease; if it is not affordable, full-dose R-CHOP is a good standard.
- Over 80 is not a contraindication to cure: a steroid pre-phase and R-mini-CHOP cure some.
- A Deauville 4–5 residue at the end of treatment needs a biopsy before it is called refractory.
- Relapse within a year of R-CHOP: think CAR-T early, because making the cells takes weeks.
- Every relapse needs a biopsy: it may be a transformed indolent lymphoma, a different lymphoma, infection or another cancer.
- No routine surveillance scans in complete remission: teach patients which symptoms to report.
- Test every patient with an aggressive lymphoma for HIV; continue antiretroviral therapy during chemotherapy.
- New neurological symptoms after rituximab: urgent MRI (CNS relapse, PML).

11 Case vignettes: lines of management

CASE 1 Limited stage · four cycles · hepatitis B

A neck node and an "inconclusive" FNA

52 years, man

Right neck, 4 cm

IPI 0

A 52-year-old shopkeeper has a painless right neck swelling that has grown over 6 weeks. An FNA elsewhere said "lymphoproliferative lesion, suggest biopsy". He has no fever, sweats or weight loss and works normally.

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: DLBCL, GCB type by Hans (CD10 positive); MYC FISH negative; EBER negative.

2

STAGE AND SCORE

PET-CT: right cervical nodes only, largest 4 cm. Stage I, LDH normal, ECOG 0, age 52: IPI 0. CNS-IPI 0. Echo normal.

3

BEFORE TREATMENT

HIV and HCV negative. HBsAg negative, anti-HBc positive, HBV DNA undetectable: entecavir prophylaxis during rituximab and for at least a year after, with hepatology.

4

TREAT

Non-bulky limited stage: R-CHOP × 3, then PET3 Deauville 2 → one more cycle, four in total (S1001; FLYER showed four cycles match six). End-of-treatment PET Deauville 1: follow-up every 3–6 months, no routine scans.

TEACHING POINTS

- FNA can only raise the suspicion; excise the node.
- Non-bulky limited stage: PET after three cycles; negative → four cycles in total.
- Anti-HBc alone carries moderate risk with rituximab: give prophylaxis.

See: Sections 03, 05 and 06, Algorithm 2.

CASE 2 Advanced · non-GCB · high CNS risk

Abdominal fullness, weight loss and a kidney mass

64 years, woman

Stage IV

IPI 5, CNS-IPI 6

A 64-year-old retired teacher has 2 months of abdominal fullness, 7 kg weight loss and night sweats. She is up and about but cannot work (ECOG 2). LDH is twice normal; uric acid is high.

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

1

DIAGNOSE

CT-guided cores of a 9 cm retroperitoneal mass: DLBCL, non-GCB; MYC and BCL2 protein high (double-expressor); FISH shows no rearrangement.

2

STAGE AND SCORE

PET-CT: retroperitoneal mass, left kidney and adrenal, bone marrow: stage IV. IPI 5. CNS-IPI 6 (age, LDH, ECOG, stage, extranodal sites, kidney/adrenal): MRI brain and lumbar puncture with flow cytometry are negative.

3

BEFORE CYCLE 1

Steroid pre-phase; IV fluids; rasburicase after a normal G6PD (bulky, high LDH and uric acid); HBV, HCV, HIV negative; echo normal; G-CSF planned.

4

TREAT

Pola-R-CHP × 6 (non-GCB, IPI 2–5; affordable through her insurance). CNS prophylaxis discussed: unproven benefit, high risk; she chooses high-dose methotrexate after systemic therapy. End-of-treatment PET Deauville 3.

TEACHING POINTS

- Kidney or adrenal disease adds a CNS-IPI point; score it on day one.
- Double-expressor is still DLBCL, NOS, but adds risk.
- Lysis prophylaxis starts before the first dose.

See: Sections O4 and O6, Figures on CNS risk and first-line evidence, Algorithms 1 and 2.

CASE 3 Over 80 · R-mini-CHOP**An 83-year-old with nodes on both sides of the diaphragm**

83 years, man

Stage III

Diabetic

An 83-year-old retired farmer with type 2 diabetes lives with his son and is independent in daily activities but walks slowly. He has had 6 weeks of tiredness and painless neck and groin nodes. Creatinine and LVEF are normal.

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

1

DIAGNOSE

Neck node excision: DLBCL, GCB type; MYC FISH negative.

2

ASSESS

PET-CT stage III; IPI 3. Simplified geriatric assessment: unfit (slow gait, several comorbidities), not frail.

3

PREPARE

Prednisolone pre-phase for a week (sugar monitored, insulin adjusted); HBV screen negative; G-CSF arranged; family taught to report fever the same day.

4

TREAT

R-mini-CHOP × 6 every 21 days. Complete metabolic response. Visits every 3 months; blood pressure and sugar with his family doctor.

TEACHING POINTS

- Age alone is not a reason to withhold curative treatment.
- Steroid pre-phase lowers first-cycle toxicity in older patients.
- R-mini-CHOP gives about 59% 2-year survival over 80.

See: Sections O3 and O6, Figure on special settings, Algorithm 2.

CASE 4 Primary mediastinal · young woman**Morning facial swelling and a wide mediastinum**

27 years, woman

Mediastinal mass 12 cm

SVC obstruction

A 27-year-old accountant has 6 weeks of dry cough and, for a week, swelling of her face and neck in the mornings. Chest X-ray shows a wide mediastinum; CT shows a 12 cm anterior mediastinal mass compressing the superior vena cava.

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

1

GET TISSUE SAFELY

Anaesthetist reviews the airway; anterior mediastinotomy biopsy before any steroid (needle cores are often crushed): primary mediastinal large B-cell lymphoma (CD20+, CD30 weak, PD-L1+, CD10-); no MYC rearrangement.

2

STAGE

PET-CT: stage II bulky. Echo normal. Fertility counselling; pregnancy test negative.

3

CHOOSE

Two acceptable options: R-CHOP × 6 then mediastinal RT, or DA-EPOCH-R × 6 without RT. The RT field would include both breasts, so she chooses DA-EPOCH-R. The SVC symptoms settle within the first cycle.

4

AFTER TREATMENT

A 4 cm residual mass, Deauville 2: no radiotherapy. Follow-up for relapse in the first two years; if she relapses early, CAR-T; later, salvage and transplant or PD-1 blockade.

TEACHING POINTS

- PMBL is a distinct entity of young adults, mostly women; a surgical biopsy is preferred.
- R-CHOP + RT and DA-EPOCH-R alone are both acceptable: choose by the RT field.
- A residual mass is common and often fibrosis: PET decides.

See: Sections O2, O5 and O6, Algorithm 3.

CASE 5 Burkitt · tumour lysis**A young man operated on for "appendicitis"**

22 years, man

Ileocaecal mass

LDH 6× normal

A 22-year-old student had 3 weeks of abdominal pain; an ileocaecal mass was found at surgery for suspected appendicitis and biopsied. Two days later his creatinine and potassium are rising.

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

1

DIAGNOSE

Burkitt lymphoma: monomorphic medium cells, starry sky, Ki-67 near 100%, CD10+, BCL2-, t(8;14) MYC::IGH. HIV negative.

2

PROTECT THE KIDNEYS

Tumour lysis: IV fluids, rasburicase after a normal G6PD test, correct potassium and phosphate; kidney team on standby.

3

STAGE

PET-CT: abdominal disease, marrow negative; lumbar puncture with flow: no CNS disease. BL-IPI 1 (LDH over three times normal). Sperm banking the same week.

4

TREAT

R-CODOX-M/R-IVAC with intrathecal prophylaxis, rituximab from cycle 2; admitted for each cycle. Complete metabolic response; visits every 3–4 months in the first year.

TEACHING POINTS

- Think Burkitt in a young man with a fast abdominal mass.
- Lysis prophylaxis and the LP come before chemotherapy.
- R-CHOP alone under-treats Burkitt; rituximab improves survival.

See: Section O6 (Burkitt), Figure on Burkitt, Algorithm 3.

CASE 6 Early relapse · CAR-T in India**New nodes seven months after R-CHOP**

47 years, man

Relapse at 7 months

Fit

A 47-year-old teacher with stage IV DLBCL had a complete response to R-CHOP × 6. Seven months later new axillary and abdominal nodes appear and his LDH rises.

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

1**CONFIRM**

Axillary node biopsy: DLBCL, CD19 positive; PET: stage III. Fit, ECOG 1.

2**CHOOSE**

Relapse within 12 months: CD19 CAR-T is preferred over salvage and transplant (ZUMA-7, TRANSFORM). In India, NexCAR19 (approved 2023); cost and insurance or scheme cover discussed with the family and the hospital.

3**BRIDGE**

Cells collected; R-GemOx while the product is made (no CD19-directed drugs before CD19 CAR-T). Infection prophylaxis.

4**AFTER CAR-T**

Grade 1 CRS (fever) on day 2 settles with paracetamol and fluids; daily ICE score stays normal. Complete metabolic response at 3 months. If CAR-T had not been possible: glofitamab-GemOx (STARGLO) or salvage then transplant.

TEACHING POINTS

- Early relapse after R-CHOP does badly with salvage chemotherapy: refer for CAR-T early.
- Know CRS (fever first) and ICANS (confusion, writing change) before you refer.
- Indian CAR-T costs about a tenth of the price abroad.

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

CASE 7 HIV-associated DLBCL**Fever, weight loss and nodes in a man just found to have HIV**

39 years, man

CD4 110

Stage IV

A 39-year-old driver has 2 months of fever, 10 kg weight loss and enlarged neck and abdominal nodes. HIV is diagnosed during the work-up (CD4 110, high viral load); he has never taken antiretroviral therapy.

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

1**DIAGNOSE**

Neck node excision: DLBCL, GCB type, EBER positive; MYC FISH negative. PET-CT stage IV; CNS-IPI 3; LP negative.

2**START HIV CARE**

Antiretroviral therapy with the HIV team, choosing drugs without major interactions; co-trimoxazole; HBV and TB screening.

3**TREAT**

CD4 above 50: rituximab is added. R-CHOP × 6 (DA-EPOCH-R is an alternative) with G-CSF. Antiretroviral therapy continues throughout.

4**OUTCOME**

Complete metabolic response; CD4 rises over the following months. Outcomes now match those of people without HIV.

TEACHING POINTS

- Test every patient with an aggressive lymphoma for HIV.
- Continue antiretroviral therapy during chemotherapy; check interactions.
- Rituximab when CD4 is 50 or more.

See: Section O6 (special settings), Figure on special settings, Algorithm 3.

12 References & guidelines

- NCCN Guidelines: B-Cell Lymphomas (current version); ESMO clinical practice guidelines for DLBCL; British Society for Haematology guidance on DLBCL; [Lugano 2014](#)^[1]; WHO Classification, 5th edition, and the International Consensus Classification (2022); ASTCT consensus grading of CRS and ICANS; ASCO provisional clinical opinion on hepatitis B screening (2020).
- Cross-checked in October 2026 against 29 UpToDate topic reviews: DLBCL presentation, diagnosis and classification; limited-stage DLBCL; advanced-stage DLBCL; first relapse or refractory DLBCL in fit patients; second or later relapse or unfit patients; prognosis of DLBCL; pathobiology of DLBCL and PMBL; primary mediastinal large B-cell lymphoma; NHL clinical presentation and initial evaluation; overview of NHL pathobiology; classification of haematopoietic neoplasms; Burkitt lymphoma diagnosis; Burkitt treatment in adults; primary CNS lymphoma treatment; secondary CNS lymphoma diagnosis and treatment; HIV-related lymphoma treatment; PTLD treatment; Richter transformation; primary cutaneous DLBCL, leg type; tumour lysis syndrome (two topics); hepatitis B reactivation; cytokine release syndrome; ICANS; principles of cancer immunotherapy; NHL in children and adolescents; chemotherapy in older adults; care of adult NHL survivors.
- Citations were taken from the UpToDate reference lists (journal, volume and first page), STARGLO and the ZUMA-7 overall survival paper were also web-verified, and the two Indian papers were confirmed against the published record on 16 October 2026 (Lancet Haematol 2025;12:e282; ecancermedicalsience 2021;15:1242). Indian facts web-verified on 16 October 2026: NexCAR19 CDSCO approval (13 October 2023) and reported price; Qartemi approval (January 2025); polatuzumab DCGL approval (September 2023, per Roche India); Tata Medical Center elderly DLBCL series. Reviewed and approved by Dr. Haritha Chiramana, 16 October 2026.

Core trials and papers cited on this page (79)

Journal, year, volume and first page (or a PubMed search); each links to the PubMed record by exact citation.

NUMBERED IN ORDER OF FIRST CITATION IN THE TEXT

1. **LNH-98.5 ten-year (Coiffier 2010)**: Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial. *Blood* 2010;116:2040. [PubMed](#) **First-line DLBCL**
2. **MInT**: Pfreundschuh M, Trümper L, Osterborg A, et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis DLBCL (MInT). *Lancet Oncol* 2006;7:379. [PubMed](#) **First-line DLBCL**
3. **POLARIX five-year**: Morschhauser F, Salles G, Sehn LH, et al. Five-year outcomes of the POLARIX study comparing Pola-R-CHP and R-CHOP. *J Clin Oncol* 2025;43:3698. [PubMed](#) **First-line DLBCL**
4. **ZUMA-7 overall survival (Westin 2023)**: Westin JR, Oluwole OO, Kersten MJ, et al. Survival with axicabtagene ciloleucel in large B-cell lymphoma. *N Engl J Med* 2023;389:148. [PubMed](#) **Relapsed or refractory disease**
5. **EFS24 (Maurer 2014)**: Maurer MJ, Ghesquières H, Jais JP, et al. Event-free survival at 24 months is a robust end point for disease-related outcome in DLBCL. *J Clin Oncol* 2014;32:1066. [PubMed](#) **Classification, pathology and prognosis**
6. **Elderly DLBCL, Tata Medical Center Kolkata (Sarker 2021)**: Sarker C, Radhakrishnan VS, Mandal P, et al. Outcomes of diffuse large B-cell lymphoma in elderly patients: real-world experience from a middle-income country setting. *ecancermedicalsience* 15:1242. 2021. doi:10.3332/ecancer.2021.1242. [PubMed](#) **India**
7. **Hans algorithm (2004)**: Hans CP, Weisenburger DD, Greiner TC, et al. Confirmation of the molecular classification of DLBCL by immunohistochemistry using a tissue microarray. *Blood* 2004;103:275. [PubMed](#) **Classification, pathology and prognosis**
8. **WHO 5th edition lymphoid (Alaggio 2022)**: Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the WHO Classification of Haematolymphoid Tumours: lymphoid neoplasms. *Leukemia* 2022;36:1720. [PubMed](#) **Classification, pathology and prognosis**
9. **International Consensus Classification (Campo 2022)**: Campo E, Jaffe ES, Cook JR, et al. The International Consensus Classification of mature lymphoid neoplasms. *Blood* 2022;140:1229. [PubMed](#) **Classification, pathology and prognosis**
10. **Simplified geriatric assessment (Merli 2021)**: Merli F, Luminari S, Tucci A, et al. Simplified geriatric assessment in older patients with DLBCL (Elderly Project). *J Clin Oncol* 2021;39:1214. [PubMed](#) **Older adults, heart disease and special settings**

11. **Lugano classification (Cheson 2014):** Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol* 2014;32:3059. [PubMed](#) Classification, pathology and prognosis
12. **IPI (1993):** International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. *N Engl J Med* 1993;329:987. [PubMed](#) Classification, pathology and prognosis
13. **IPI in the rituximab era (Ziepert 2010):** Ziepert M, Hasenclever D, Kuhnt E, et al. Standard IPI remains a valid predictor of outcome in aggressive CD20+ B-cell lymphoma in the rituximab era. *J Clin Oncol* 2010;28:2373. [PubMed](#) Classification, pathology and prognosis
14. **NCCN-IPI (Zhou 2014):** Zhou Z, Sehn LH, Rademaker AW, et al. An enhanced International Prognostic Index (NCCN-IPI) for DLBCL treated in the rituximab era. *Blood* 2014;123:837. [PubMed](#) Classification, pathology and prognosis
15. **Cell of origin by Lymph2Cx (Scott 2015):** Scott DW, Mottok A, Ennishi D, et al. Prognostic significance of DLBCL cell of origin determined by digital gene expression in FFPE biopsies. *J Clin Oncol* 2015;33:2848. [PubMed](#) Classification, pathology and prognosis
16. **MYC partner gene (Rosenwald 2019):** Rosenwald A, Bens S, Advani R, et al. Prognostic significance of MYC rearrangement and translocation partner in DLBCL. *J Clin Oncol* 2019;37:3359. [PubMed](#) Classification, pathology and prognosis
17. **MYC and BCL2 co-expression (Johnson 2012):** Johnson NA, Slack GW, Savage KJ, et al. Concurrent expression of MYC and BCL2 in DLBCL treated with R-CHOP. *J Clin Oncol* 2012;30:3452. [PubMed](#) Classification, pathology and prognosis
18. **ctDNA remission assessment (Roschewski 2025):** Roschewski M, Kurtz DM, Westin JR, et al. Remission assessment by circulating tumor DNA in large B-cell lymphoma. *J Clin Oncol* 2025;43:3652. [PubMed](#) First-line DLBCL
19. **LYSA/GOELAMS 02-03 (Lamy 2018):** Lamy T, Damaj G, Soubeyran P, et al. R-CHOP 14 with or without radiotherapy in nonbulky limited-stage DLBCL. *Blood* 2018;131:174. [PubMed](#) First-line DLBCL
20. **IELSG-10 testicular (Vitolo 2011):** Vitolo U, Chiappella A, Ferreri AJ, et al. First-line treatment for primary testicular DLBCL with R-CHOP, CNS prophylaxis, and contralateral testis irradiation. *J Clin Oncol* 2011;29:2766. [PubMed](#) First-line DLBCL
21. **Consolidation RT meta-analysis (Berger 2021):** Berger MD, Trelle S, Büchi AE, et al. Impact on survival through consolidation radiotherapy for DLBCL: a comprehensive meta-analysis. *Haematologica* 2021;106:1923. [PubMed](#) First-line DLBCL
22. **IELSG-26 PET in PMBL (Martelli 2014):** Martelli M, Ceriani L, Zucca E, et al. [18F]fluorodeoxyglucose PET predicts survival after chemioimmunotherapy for primary mediastinal large B-cell lymphoma (IELSG-26). *J Clin Oncol* 2014;32:1769. [PubMed](#) Older adults, heart disease and special settings
23. **S1001 (Persky 2020):** Persky DO, Li H, Stephens DM, et al. Positron emission tomography-directed therapy for patients with limited-stage DLBCL (SWOG S1001). *J Clin Oncol* 2020;38:3003. [PubMed](#) First-line DLBCL
24. **FLYER:** Poeschel V, Held G, Ziepert M, et al. Four versus six cycles of CHOP chemotherapy in combination with six applications of rituximab in younger patients with favourable DLBCL (FLYER). *Lancet* 2019;394:2271. [PubMed](#) First-line DLBCL
25. **R-CHOP vs CHOP, GELA LNH-98.5 (Coiffier 2002):** Coiffier B, Lepage E, Briere J, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with DLBCL. *N Engl J Med* 2002;346:235. [PubMed](#) First-line DLBCL
26. **E4494 (Habermann 2006):** Habermann TM, Weller EA, Morrison VA, et al. Rituximab-CHOP versus CHOP alone or with maintenance rituximab in older patients with DLBCL. *J Clin Oncol* 2006;24:3121. [PubMed](#) First-line DLBCL
27. **MInT six-year:** Pfreundschuh M, Kuhnt E, Trümper L, et al. Six-year results of the MabThera International Trial. *Lancet Oncol* 2011;12:1013. [PubMed](#) First-line DLBCL
28. **POLARIX:** Tilly H, Morschhauser F, Sehn LH, et al. Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma. *N Engl J Med* 2022;386:351. [PubMed](#) First-line DLBCL
29. **RICOVER-60:** Pfreundschuh M, Schubert J, Ziepert M, et al. Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients (RICOVER-60). *Lancet Oncol* 2008;9:105. [PubMed](#) First-line DLBCL
30. **R-CHOP-14 vs R-CHOP-21 (Cunningham 2013):** Cunningham D, Hawkes EA, Jack A, et al. R-CHOP in newly diagnosed DLBCL: 14-day versus 21-day cycles. *Lancet* 2013;381:1817. [PubMed](#) First-line DLBCL
31. **LNHO3-6B:** Delarue R, Tilly H, Mounier N, et al. Dose-dense R-CHOP compared with standard R-CHOP in elderly patients with DLBCL (LNHO3-6B). *Lancet Oncol* 2013;14:525. [PubMed](#) First-line DLBCL
32. **CALGB 50303:** Bartlett NL, Wilson WH, Jung SH, et al. Dose-adjusted EPOCH-R compared with R-CHOP as frontline therapy for DLBCL (Alliance/CALGB 50303). *J Clin Oncol* 2019;37:1790. [PubMed](#) First-line DLBCL
33. **PETAL:** Dührsen U, Müller S, Hertenstein B, et al. PET-guided therapy of aggressive non-Hodgkin lymphomas (PETAL). *J Clin Oncol* 2018;36:2024. [PubMed](#) First-line DLBCL
34. **Lenalidomide maintenance, REMARC:** Thieblemont C, Tilly H, Gomes da Silva M, et al. Lenalidomide maintenance compared with placebo in responding elderly patients with DLBCL. *J Clin Oncol* 2017;35:2473. [PubMed](#) First-line DLBCL
35. **R-mini-CHOP (Peyrade 2011):** Peyrade F, Jardin F, Thieblemont C, et al. Attenuated immunochemotherapy regimen (R-miniCHOP) in patients older than 80 years with DLBCL. *Lancet Oncol* 2011;12:460. [PubMed](#) Older adults, heart disease and special settings

36. **R-CEOP (Moccia 2021)**: Moccia AA, Schaff K, Freeman C, et al. Long-term outcomes of R-CEOP in DLBCL with a contraindication to anthracyclines. *Blood Adv* 2021;5:1483. [PubMed](#) Older adults, heart disease and special settings
37. **R-GCVP (Fields 2014)**: Fields PA, Townsend W, Webb A, et al. De novo treatment of DLBCL with R-GCVP in patients with cardiac comorbidity. *J Clin Oncol* 2014;32:282. [PubMed](#) Older adults, heart disease and special settings
38. **High-dose methotrexate prophylaxis (Lewis 2023)**: Lewis KL, Jakobsen LH, Villa D, et al. High-dose methotrexate as CNS prophylaxis in high-risk aggressive B-cell lymphoma. *J Clin Oncol* 2023;41:5376. [PubMed](#) First-line DLBCL
39. **CNS-IPI (Schmitz 2016)**: Schmitz N, Zeynalova S, Nickelsen M, et al. CNS International Prognostic Index: a risk model for CNS relapse in DLBCL treated with R-CHOP. *J Clin Oncol* 2016;34:3150. [PubMed](#) Classification, pathology and prognosis
40. **DA-EPOCH-R in PMBL (Dunleavy 2013)**: Dunleavy K, Pittaluga S, Maeda LS, et al. Dose-adjusted EPOCH-rituximab therapy in primary mediastinal B-cell lymphoma. *N Engl J Med* 2013;368:1408. [PubMed](#) Older adults, heart disease and special settings
41. **Pembrolizumab in relapsed PMBL (Armand 2019)**: Armand P, Rodig S, Melnichenko V, et al. Pembrolizumab in relapsed or refractory primary mediastinal large B-cell lymphoma. *J Clin Oncol* 2019;37:3291. [PubMed](#) Older adults, heart disease and special settings
42. **Nivolumab + brentuximab in PMBL (Zinzani 2019)**: Zinzani PL, Santoro A, Gritti G, et al. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large B-cell lymphoma (CheckMate 436). *J Clin Oncol* 2019;37:3081. [PubMed](#) Older adults, heart disease and special settings
43. **Rituximab in adult Burkitt (Ribrag 2016)**: Ribrag V, Koscielny S, Bosq J, et al. Rituximab and dose-dense chemotherapy for adults with Burkitt's lymphoma: a randomised phase 3 trial. *Lancet* 2016;387:2402. [PubMed](#) Burkitt lymphoma and children
44. **GMALL Burkitt (Hoelzer 2014)**: Hoelzer D, Walewski J, Döhner H, et al. Improved outcome of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy. *Blood* 2014;124:3870. [PubMed](#) Burkitt lymphoma and children
45. **DA-EPOCH-R in Burkitt (Roschewski 2020)**: Roschewski M, Dunleavy K, Abramson JS, et al. Risk-adapted therapy with dose-adjusted EPOCH-R in adults with untreated Burkitt lymphoma. *J Clin Oncol* 2020;38:2519. [PubMed](#) Burkitt lymphoma and children
46. **HOVON/SAKK Burkitt (Chamuleau 2023)**: Chamuleau MED, Stenner F, Chitu DA, et al. R-CODOX-M/R-IVAC versus DA-EPOCH-R in newly diagnosed Burkitt lymphoma (HOVON/SAKK). *Lancet Haematol* 2023;10:e966. [PubMed](#) Burkitt lymphoma and children
47. **BL-IPI (Olszewski 2021)**: Olszewski AJ, Jakobsen LH, Collins GP, et al. Burkitt Lymphoma International Prognostic Index. *J Clin Oncol* 2021;39:1129. [PubMed](#) Burkitt lymphoma and children
48. **Inter-B-NHL Ritux 2010 (Minard-Colin 2020)**: Minard-Colin V, Aupérin A, Pillon M, et al. Rituximab for high-risk, mature B-cell non-Hodgkin's lymphoma in children. *N Engl J Med* 2020;382:2207. [PubMed](#) Burkitt lymphoma and children
49. **MATRIx/IELSG32 (Ferrerri 2016)**: Ferreri AJ, Cwynarski K, Pulczynski E, et al. Chemoimmunotherapy with methotrexate, cytarabine, thiotepa and rituximab (MATRIx) for primary CNS lymphoma (IELSG32). *Lancet Haematol* 2016;3:e217. [PubMed](#) Older adults, heart disease and special settings
50. **PRECIS (Houillier 2019)**: Houillier C, Taillandier L, Dureau S, et al. Radiotherapy or autologous stem-cell transplantation for primary CNS lymphoma in patients 60 years of age and younger (PRECIS). *J Clin Oncol* 2019;37:823. [PubMed](#) Older adults, heart disease and special settings
51. **MATRIx/IELSG43 (Illerhaus 2026)**: Illerhaus G, Ferreri AJM, Wendler J, et al. High-dose chemotherapy with autologous transplantation versus conventional chemotherapy consolidation in primary CNS lymphoma (MATRIx/IELSG43). *Lancet* 2026;408:532. [PubMed](#) Older adults, heart disease and special settings
52. **MARIETTA (Ferrerri 2021)**: Ferreri AJM, Doorduijn JK, Re A, et al. MATRIx-RICE therapy and autologous haematopoietic stem-cell transplantation in DLBCL with secondary CNS involvement (MARIETTA). *Lancet Haematol* 2021;8:e110. [PubMed](#) Older adults, heart disease and special settings
53. **HIV-NHL pooled analysis (Barta 2013)**: Barta SK, Xue X, Wang D, et al. Treatment factors affecting outcomes in HIV-associated non-Hodgkin lymphomas: a pooled analysis of 1546 patients. *Blood* 2013;122:3251. [PubMed](#) Older adults, heart disease and special settings
54. **Venetoclax + DA-EPOCH-R in Richter (Davids 2022)**: Davids MS, Rogers KA, Tyekucheva S, et al. Venetoclax plus dose-adjusted R-EPOCH for Richter syndrome. *Blood* 2022;139:686. [PubMed](#) Older adults, heart disease and special settings
55. **PTLD-1 (Trappe 2012)**: Trappe R, Oertel S, Leblond V, et al. Sequential treatment with rituximab followed by CHOP in adult B-cell PTLD (PTLD-1). *Lancet Oncol* 2012;13:196. [PubMed](#) Older adults, heart disease and special settings
56. **PTLD-1 risk-stratified (Trappe 2017)**: Trappe RU, Dierickx D, Zimmermann H, et al. Response to rituximab induction allows stratification into rituximab or R-CHOP consolidation in B-cell PTLD. *J Clin Oncol* 2017;35:536. [PubMed](#) Older adults, heart disease and special settings
57. **PCDLBCL leg type (Grange 2007)**: Grange F, Beylot-Barry M, Courville P, et al. Primary cutaneous DLBCL, leg type: clinicopathologic features and prognostic analysis in 60 cases. *Arch Dermatol* 2007;143:1144. [PubMed](#) Older adults, heart disease and special settings

58. **SCHOLAR-1:** Crump M, Neelapu SS, Farooq U, et al. Outcomes in refractory DLBCL: results from the international SCHOLAR-1 study. *Blood* 2017;130:1800. [PubMed](#) Relapsed or refractory disease
59. **ZUMA-7:** Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene ciloleucel as second-line therapy for large B-cell lymphoma. *N Engl J Med* 2022;386:640. [PubMed](#) Relapsed or refractory disease
60. **TRANSFORM:** Kamdar M, Solomon SR, Arnason J, et al. Lisocabtagene maraleucel versus standard of care as second-line therapy for large B-cell lymphoma (TRANSFORM). *Lancet* 2022;399:2294. [PubMed](#) Relapsed or refractory disease
61. **BELINDA:** Bishop MR, Dickinson M, Purtill D, et al. Second-line tisagenlecleucel or standard care in aggressive B-cell lymphoma (BELINDA). *N Engl J Med* 2022;386:629. [PubMed](#) Relapsed or refractory disease
62. **CORAL:** Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. *J Clin Oncol* 2010;28:4184. [PubMed](#) Relapsed or refractory disease
63. **TRANSCEND (Abramson 2020):** Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001). *Lancet* 2020;396:839. [PubMed](#) Relapsed or refractory disease
64. **Glofitamab monotherapy (Dickinson 2022):** Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory DLBCL. *N Engl J Med* 2022;387:2220. [PubMed](#) Relapsed or refractory disease
65. **Epcoritamab, EPCORE NHL-1 (Thieblemont 2023):** Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab in relapsed or refractory large B-cell lymphoma (EPCORE NHL-1). *J Clin Oncol* 2023;41:2238. [PubMed](#) Relapsed or refractory disease
66. **STARGLO:** Abramson JS, Ku M, Hertzberg M, et al. Glofitamab plus gemcitabine and oxaliplatin versus rituximab-GemOx for relapsed or refractory DLBCL (STARGLO). *Lancet* 2024;404:1940. [PubMed](#) Relapsed or refractory disease
67. **Pola-BR (Sehn 2020):** Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab vedotin in relapsed or refractory DLBCL. *J Clin Oncol* 2020;38:155. [PubMed](#) Relapsed or refractory disease
68. **L-MIND (Salles 2020):** Salles G, Duell J, González Barca E, et al. Tafasitamab plus lenalidomide in relapsed or refractory DLBCL (L-MIND). *Lancet Oncol* 2020;21:978. [PubMed](#) Relapsed or refractory disease
69. **LOTIS-2 (Caimi 2021):** Caimi PF, Ai W, Alderuccio JP, et al. Loncastuximab tesirine in relapsed or refractory DLBCL (LOTIS-2). *Lancet Oncol* 2021;22:790. [PubMed](#) Relapsed or refractory disease
70. **Tumour lysis guidelines (Coiffier 2008):** Coiffier B, Altman A, Pui CH, et al. Guidelines for the management of pediatric and adult tumor lysis syndrome. *J Clin Oncol* 2008;26:2767. [PubMed](#) Supportive care, follow-up and late effects
71. **Entecavir vs lamivudine prophylaxis (Huang 2014):** Huang H, Li X, Zhu J, et al. Entecavir vs lamivudine for prevention of hepatitis B reactivation among patients with untreated DLBCL receiving R-CHOP. *JAMA* 2014;312:2521. [PubMed](#) Supportive care, follow-up and late effects
72. **ASCO HBV screening and management (Hwang 2020):** Hwang JP, Feld JJ, Hammond SP, et al. Hepatitis B virus screening and management for patients with cancer prior to therapy: ASCO provisional clinical opinion update. *J Clin Oncol* 2020;38:3698. [PubMed](#) Supportive care, follow-up and late effects
73. **NexCAR19 pivotal trial (India):** Jain H, Karulkar A, Kalra D, et al. Talicabtagene autoleucel (NexCAR19) for relapsed or refractory B-cell malignancies: results from an open-label, multicentre, phase 1/2 study. *Lancet Haematol* 2025;12:e282. [PubMed](#) India
74. **Surveillance imaging (Thompson 2014):** Thompson CA, Ghesquieres H, Maurer MJ, et al. Utility of routine post-therapy surveillance imaging in DLBCL. *J Clin Oncol* 2014;32:3506. [PubMed](#) Supportive care, follow-up and late effects
75. **Routine imaging, Danish-Swedish (El-Galaly 2015):** El-Galaly TC, Jakobsen LH, Hutchings M, et al. Routine imaging for DLBCL in first complete remission does not improve post-treatment survival. *J Clin Oncol* 2015;33:3993. [PubMed](#) Supportive care, follow-up and late effects
76. **Heart disease after DLBCL treatment (Geurts 2026):** Geurts YM, Neppelenbroek SIM, Aleman BMP, et al. Cardiovascular disease risk after radiotherapy and anthracycline-based chemotherapy for DLBCL. *J Natl Cancer Inst* 2026;118:1628. [PubMed](#) Supportive care, follow-up and late effects
77. **Heart disease after aggressive NHL (Moser 2006):** Moser EC, Noordijk EM, van Leeuwen FE, et al. Long-term risk of cardiovascular disease after treatment for aggressive non-Hodgkin lymphoma. *Blood* 2006;107:2912. [PubMed](#) Supportive care, follow-up and late effects
78. **Second cancers by NHL subtype (Morton 2010):** Morton LM, Curtis RE, Linet MS, et al. Second malignancy risks after non-Hodgkin's lymphoma and CLL: differences by lymphoma subtype. *J Clin Oncol* 2010;28:4935. [PubMed](#) Supportive care, follow-up and late effects
79. **PML after rituximab (Carson 2009):** Carson KR, Evens AM, Richey EA, et al. Progressive multifocal leukoencephalopathy after rituximab therapy in HIV-negative patients. *Blood* 2009;113:4834. [PubMed](#) Supportive care, follow-up and late effects

Educational summary for health professionals, written in our own words from current guidelines and primary trials. No drug doses are given. Hodgkin lymphoma is covered in part 1; indolent B-cell lymphomas, T-cell 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.