Lancashire and South Cumbria Haematology Guideline for Large B-cell Lymphoma (LBCL) – February 2026

Contents

1. Scope
2. Pre, interim and post-treatment evaluation
3. Management of DLBCL (NOS) including T-cell/histiocyte rich, EBV-positive LBCL and LBCL with IRF4 rearrangement
4. Management of high grade B-cell lymphoma with myc and bcl-2 (+/- bcl-6) rearrangements ('double/triple hit')
5. Management of older or less fit patients
6. Management of primary DLBCL at extranodal sites
7. Management of DLBCL presenting with synchronous systemic and CNS DLBCL
8. CNS prophylaxis for DLBCL
9. Management of relapsed and refractory DLBCL and 'double/triple hit' lymphoma
10. Management of relapsed DLBCL with secondary CNS involvement
11. Management of LBCL with 11q aberration
12. Management of high grade B-cell lymphoma (HGBL) (NOS)

Appendix 1: IPI and NCCN-IPI score
Appendix 2: CNS IPI risk score
Appendix 3: Second-line IPI score

1 Scope

This guideline covers the management of:

- Diffuse large B-cell lymphoma, NOS (DLBCL-NOS)
- T-cell/histiocyte rich large B-cell lymphoma
- EBV-positive large B-cell lymphoma, NOS
- Large B-cell lymphoma with IRF4
- Large B-cell lymphoma of extranodal sites (excluding CNS)
- HGBL with myc and bcl-2 (+/-bcl-6) rearrangements
- HGBL with myc and bcl-6 rearrangements
- Large B-cell lymphoma (LBCL) with 11q aberration
- High grade B-cell lymphoma (NOS)

The following are beyond the scope of this guideline:

- Burkitt's lymphoma
- Post-transplant B-cell lymphoproliferative disorders
- B-cell lymphoma in patients with HIV infection
- Primary mediastinal B-cell lymphoma
- Mediastinal grey-zone lymphoma
- Primary CNS lymphoma
- Plasmablastic lymphoma
- EBC-positive mucocutaneous ulcer
- Nodular lymphocyte-predominant Hodgkin's lymphoma
- High grade transformation of low grade B-cell lymphoma

2 Pretreatment evaluation

2.1
- The diagnosis should be made on a lymph node excision biopsy, or when this is not possible, at least a good quality needle core biopsy.
- Management will be based on the diagnosis made following expert haematopathology review at HMDS Leeds

2.2 The following investigations should be performed prior to deciding treatment:
- FBC, U&Es, creat, LFTs, calcium, LDH, urate, phosphate, immunoglobulins/serum electrophoresis
- Hepatitis B, C and HIV serology
- PET-CT scan if feasible and where treatment is with curative intent. Otherwise contrast-enhanced CT scan neck, thorax and abdomen. Note a CT scan is not usually necessary if PET-CT is available but may be helpful in delineating disease at some sites e.g intra-abdominal.
- MRI scan for assessment of disease in the oropharynx and Waldeyer's ring, sinuses and nasal cavity, and paraspinal areas where there is a suspicion of spinal cord compromise
- Consider bone marrow aspirate and trephine biopsy – although PET-CT has largely replaced routine marrow examination, it may miss low volume disease or low grade lymphoma hence biopsy may be indicated if this would influence management decisions regarding treatment decisions e.g change in prognostic score, staging of apparent early stage disease.
- CT +/- MRI scan brain +/- spinal cord, and CSF examination where the patient is at high risk of CNS lymphoma, unless this would lead to undue delay in starting treatment where there is an urgent need (see section 11.0).
- For gastric lymphoma a breath or stool antigen test where H. pylori has not been identified on biopsy.
- Determination of Ann Arbor stage, presence of bulk disease >7.5cm, extranodal sites.
- Determination of the IPI, NCCN-IPI (appendix 1) and CNS-IPI (appendix 3).
- Note the cell of origin determined by immunohistochemistry i.e germinal centre or post-germinal centre phenotype, should be noted.
- ECG, chest X-ray. In patients >60 years or with a history of or risk factors for cardiac disease or when mediastinal irradiation may be indicated, assess cardiac function by MUGA scan or echocardiography

2.3 Interim and post-treatment evaluation

- There should be a formal assessment of response after four cycles of chemotherapy. If this cannot be done clinically, e.g absence of palpable disease, a CT scan should be performed.
- On completion of treatment the patient must be reassessed clinically and, where treatment is given with curative intent, all abnormal tests at baseline repeated followed by MDT discussion with review of an end of treatment PET-CT scan performed at least 6 weeks after the last dose of chemotherapy, or three months after the last dose of radiotherapy.

- In selected cases, e.g bulk disease, extranodal sites, the MDT must consider the role of consolidation radiotherapy (RT) in the presence of a Radiation Oncologist.
- There should be repeat biopsy or at least close follow up of residual FDG-avid lesions with repeat PET-CT scan before additional treatment.

2.4
- Where appropriate patients must be offered referral for reproductive counselling, and sperm cryopreservation/oocyte harvesting/ovarian preservation prior to commencing potentially gonadotoxic therapy.

2.5
- All new and relapsed cases must be discussed at the regional Lymphoma MDT prior to commencing treatment. If there is an urgent need to start treatment prior to the next MDT, the case must be discussed with an MDT Core Member.

3.0 Management of DLBCL (NOS) including T-cell/histiocyte rich, EBV-positive LBCL and LBCL with IRF4 rearrangement

3.1 Stage I and II disease

3.1.1
- Although a combined modality approach with abbreviated RCHOP and involved site radiotherapy (ISRT) is often recommended, it should be noted that there is no clear benefit demonstrable over treatment with RCHOP alone.
- For patients with low risk IPI and without bulk disease, an interim PET (iPET) response-adapted approach is feasible. This is an option especially if it is desirable to reduce exposure to chemotherapy or RT.
- Outcomes in patients with adverse risk factors, e.g IPI ≥ 2, bulk disease, remain suboptimal following abbreviated RCHOP plus ISRT, and there is no apparent benefit in the addition of RT following full course RCHOP. Note that treatment as for advanced stage disease with pola-RCHP is an option in these cases.

3.1.2 iPET adapted treatment approaches:
- For the small group 18-60 years with aaIPI 0 and no bulk, offer RCHOP x 4, followed by two cycles rituximab alone, without RT.
- For patients 61-80 years, aaIPI 0, no bulk, consider PET-directed therapy aiming to avoid routine RT: RCHOP x 2 followed by iPET. If Deauville score (DS) 0-3, for further RCHOP x 2 and no RT. If DS 4-5, for further RCHOP x 4 plus ISRT 30Gy.

3.1.3 For patients < 80 years, IPI 0-1, no bulk, consider a combined modality approach:
- RCHOP x 3-4 cycles, then ISRT 30Gy
- Or RCHOP x 6 only if it is desirable to omit RT

3.1.4 Patients with bulk disease or IPI ≥ 2:
- RCHOP or polaRCHP x 6 cycles
- Consider consolidation ISRT 30Gy according to end of treatment PET result, presence of bulk disease and after consideration of risks of RT.

3.1.5 Radiotherapy in early stage disease

- Consider 30Gy RT consolidation if there was bulk disease, residual metabolic changes on end of treatment scan, treatment with less than full dose RCHOP or non-anthracycline-based regimens, or for specific extranodal sites (see 6.0)

3.2 Management of stage III and IV disease

3.2.1 Stage III/IV, IPI 1:

- For RCHOP x 6 cycles

3.2.2 Stage III/IV, with IPI ≥ 2, ECOG ≤ 2:

- For polaRCHOP or RCHOP x 6 cycles

3.2.3 RCODOX-M/R-IVAC:

- Consider this option for patients <50-60yrs with good performance status and organ function, and IPI ≥ 3, especially if there is a concern regarding the risk of CNS disease e.g due to a high risk CNS-IPI, or the site of disease.

3.2.4 RT in patients with advanced stage disease:

- ISRT 30Gy should be considered to sites of bulk disease, residual metabolic changes on end of treatment PET-CT scan or certain extranodal sites (see 6.0).

4.0 Management of high grade B-cell lymphoma with myc and bcl-2 (+/-bcl-6) rearrangements ('double/triple hit')

- Note that the optimal therapy for this form of LBCL is uncertain, there is no standard of care and this must be discussed with the patient.
- Note that the adverse prognostic effect of myc and bcl-2 (+/- bcl-6) rearrangements is only seen when the myc translocation has an IGH or IGL gene partner.
- The prognosis for patients with early stage or low/low-intermediate risk IPI does not appear to be affected by the presence of myc and blc-2/cl-6 rearrangements.
- In patients with advanced stage/higher risk IPI treated with RCHOP outcomes appear to be poor but may be improved in younger patients treated with more intensive regimens.
- Subgroup analysis of the POLARIX trial showed that outcomes were significantly adversely affected when treated with polaRCHP compared to RCHOP.

4.1 Patients with IPI 0-2:

- RCHOP x 3-6 depending on stage +/- ISRT 30Gy

4.2 Patients with IPI 3-5

- Options are RCHOP x 6 cycles, or in younger, fit patients consider DA-R-EPOCH x 6 or RCODOX-M/R-IVAC x 2 cycles depending on clinical features, age, fitness, presence of CNS disease or risk of CNS relapse, or histopathological features, e.g high Ki67, Burkitt's-like immunophenotype.

4.3 Consider RT consolidation as for DLBCL (NOS)

4.4 Management of high grade B-cell lymphoma with myc and bcl-6 rearrangements

- This forms ~10% 'double/triple hit' LBCLs, shows greater biological heterogeneity than double hit with bcl-2 rearrangement and is not regarded as a definite biological entity in current lymphoma classifications.
- The prognosis when treated with RCHOP appears to be better than for 'double hit' with myc and bcl-2 rearrangements.
- Note that the optimal therapy for this form of LBCL is uncertain, there is no standard of care and this must be discussed with the patient.
- Treatment as for DLBCL (NOS) is appropriate, or in younger, fit patients consider treatment as for high grade B-cell lymphoma with myc and bcl-2 (+/- bcl-6) rearrangements (see 5.0).

5.0 Treatment of older, less fit or patients unfit for anthracyclines

5.1
- Note that there is a marked heterogeneity in fitness and comorbidity in older patients which is not reflected in traditional IPI scores. Using an age cut-off of 70 years rather than 60 in the IPI is better able to discriminate prognostic groups. However treatment stratification using age alone is inaccurate in predicting outcomes.
- Formalised geriatric assessment (GA) is better than clinical judgement alone in identifying older patients who may benefit from full or attenuated dose treatment. Consider using a validated frailty scoring system, e.g Elderly IPI (which incorporates simplified GA (ADLs, IADLs, CIRS-G score) plus IPI score and Hb ><12 to identify low, intermediate and high risk groups with significantly different outcomes).
- It is possible to give full-dose R-CHOP to many older patients with good performance status and good cardiac function, especially when given with primary GCSF prophylaxis.
- Note that full-dose therapy is associated with improved outcomes, at least in patients 60-80 years old.
- For patients > 80 years or unfit for 100% RCHOP prolonged survival over 2-3 years is possible with miniRCHOP.
- For patients > 80 years outcomes with 100% RCHOP and miniRCHOP may be equivalent.

5.2 Where 100% RCHOP is not appropriate due to age, comorbidities or poor performance status:
- Options are attenuated RCHOP e.g 75% dose, or 50% dose (RminiCHOP)
- Consider RT consolidation where feasible

5.3 Patients >80 years
- Consider RminiCHOP rather than 100% RCHOP depending on age, performance status, comorbidities and patient choice.
  Consider RT consolidation where feasible.

5.4 Patients for whom anthracyclines are contraindicated
- Options are R-CEOP, R-CVP, R-GCVP
- Consider consolidation RT where feasible

5.5 For frail patients:

- Options are R-CVP, low dose oral etoposide, DEC, steroids, RT for alleviation of symptoms, palliative management/supportive care alone.

6.0 Primary DLBCL at extranodal sites

6.1 Testicular lymphoma:

- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score with one dose of intrathecal methotrexate with each of cycles 1-4.
- Then high dose methotrexate 1.5-3.5g/m^2 for two doses.
- Then prophylactic scrotal radiotherapy 30Gy.

6.2 Primary breast lymphoma:

- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score.
- The role of CNS prophylaxis is uncertain but high dose methotrexate should be considered (see section 11.0).
- Consolidation RT 30Gy to the breast should be considered although it is unclear whether this improves outcomes for patients in metabolic complete remission following chemotherapy.

6.3 Primary gastric lymphoma:

- Surgery is only indicated if there is obstruction, perforation or severe bleeding.
- Antibiotic therapy in H. pylori positive cases
- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score
- End of treatment gastroscopy
- Consolidation RT 30Gy to the stomach should be considered although it is unclear whether this improves outcomes for patients in complete remission following chemotherapy.

6.4 Primary bone lymphoma:

- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score.
- Consolidation RT 30Gy should be considered although it is unclear whether this improves outcomes for patients in complete remission following chemotherapy.

6.5 Cutaneous LBCL, leg type:

- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score.
- Consolidation RT 30Gy where there is localised disease.

6.6 Intravascular large B-cell lymphoma:

- This form often involves the CNS so for MRI brain and CSF examination.
- RCHOP x 6 cycles or polaRCHP x 6 cycles according to IPI score.
- Consider intensive regimens incorporating CNS-directed agents e.g six cycles RCHOP + high dose methotrexate, RCODOX-M-R-IVAC x 2 cycles.
- Note there is a reaction of severe infusion-related reactions with the first dose of rituximab hence consider delaying this.

7.0 Management of DLBCL presenting with synchronous systemic and CNS involvement

7.1
- Biopsy of a cerebral lesion is not mandatory if biopsy of a systemic lesion has confirmed LBCL and MRI shows features consistent with CNS lymphoma. Biopsy should be considered if a CNS lesion has failed to respond to initial treatment.
- An initial cycle of RCHOP may be given if immediate control of systemic disease is required.
- In patient with poor performance status consider an initial cycle of rituximab and high dose MTX (HDMTX) then reassess performance status and fitness for MATRIX.
- If treated with MATRIX consider 50-57% reduction of cytarabine dose in cycle one for patients > 60 years or with poor performance status.
- Outcomes are improved if responses are consolidated with high dose therapy and autologous stem cell transplant (ASCT). If receiving MATRIX plan for peripheral blood mobilisation during cycle 2.

7.2
- If < 70 years and considered sufficiently fit for high dose therapy consider MATRIX + R-ICE (MARIETTA) regimen. Repeat MRI brain after two and four cycles, and PET-CT after cycle 4. If in CR or good PR offer consolidation with BCNU-thiotepa ASCT.

7.3
- In fit patients <50-60 years also consider R-CODOX-M/R-IVAC x 2 cycles, without consolidation autologous transplant.

7.4 If > 70 years or unfit for MATRIX treatment options are:
- Dose-adjusted R-MTX-cytarabine (MARTA regimen) x 2 cycles, followed by MRI brain and PET-CT scan. Although it is possible to achieve CR with respect to both CNS and systemic disease, consider additional treatment with 2-3 cycles dose-adjusted R-ICE. Offer consolidation with BCNU-thiotepa ASCT in patient achieving CR or PR.
- RCHOP x 6 cycles with intercalated HD MTX in cycles 1-4
- RCHOP x 6 cycles + intrathecal methotrexate +/- cytarabine if there is only leptomeningeal disease.
- Palliative management with steroids, RT for frail, unfit patients.

8.0 CNS prophylaxis in DLBCL

8.1
- It must be noted that, except for testicular lymphoma, there remains considerable uncertainty regarding which patients are at high risk of CNS relapse and thereby should be offered prophylaxis. Furthermore it has not yet been demonstrated that any form of prophylaxis reduces the risk of CNS relapse, other than for testicular lymphoma. These uncertainties, together with the risks of prophylaxis, must be discussed with the patient.
- Where it is considered that the patient is at high risk of secondary CNS disease or later relapse, CT +/- MRI of brain and CSF examination should be undertaken at first diagnosis if this does not cause undue delay in starting chemotherapy.
- The following scenarios are considered to be at high risk of secondary CNS lymphoma in patients with DLBCL: CNS-IPI score 5-6, ≥ 3 sites of extranodal disease, disease of testes, renal/adrenal, breast, uterus/ovary.

- CNS prophylaxis will be with high dose methotrexate 1.5-3.5g/m^2 for two cycles. This will be given after completion of initial polaRCHP/RCHOP and only when complete metabolic response has been demonstrated. Note that patients with testicular lymphoma will receive intrathecal chemotherapy also (see 9.1).
- CNS prophylaxis should also be offered if there is a concern that disease in proximity to the CNS has breached the dura. Intercalated RCHOP-high dose methotrexate (HD MTX) should be considered in these cases.
- Intrathecal chemotherapy will be used only for clearance of leptomeningeal disease when diagnosed and symptom relief.

9.0 Management of relapsed/refractory DLBCL and 'double/triple hit' lymphoma

9.1 Pretreatment evaluation

- For relapsing patients repeat biopsy should be obtained where possible, especially where relapse is late, i.e > 2 years from first CR, the patient is a candidate for high dose or CAR-T cell therapy, to exclude relapse with indolent lymphoma, or if there was uncertainty over the initial histological diagnosis, e.g diagnosis made on suboptimal tissue.
- Expression of CD20 should be noted, as well as CD79b where treatment with polatuzumab is an option, and CD19 prior to CD19-directed CAR-T cell therapy.
- Patients should be restaged with a PET scan or if this is not possible with a CT scan and bone marrow examination if considered fit enough for high dose or CAR-T cell therapy.
- CT/MRI of brain and CSF examination must be considered according to the risk of CNS disease (see 8.0).
- The second-line age-adjusted IPI (appendix 4) and time to relapse from last dose of first-line treatment should be calculated for patients considered fit for transplant/CAR-T cell therapy.
- Performance status and fitness for intensive therapy, e.g assessment of cardiac and respiratory function, must be documented.

9.2 Fit patients <80 years with refractory disease or relapsing within 12 months of last dose first-line RCHOP/polaRCHP who are candidates for intensive therapy:

- Offer referral to a CAR-T cell therapy centre at the earliest opportunity.
- If immediate treatment is indicated decisions regarding bridging therapy must be made after discussion with the CAR-T cell therapy centre.
- Note that patients relapsing/refractory with synchronous or isolated CNS lymphoma are ineligible for CAR-T cell therapy at time of writing.

9.3 Fit patients < 70-75 years relapsing > 12 months from last dose of RCHOP/polaRCHP who are candidates for high dose chemotherapy and ASCT:

- Note these patients are ineligible for CAR-T cell therapy.
- Initial treatment should be two cycles salvage chemotherapy with R-GDP followed by repeat PET-CT scan.
- If in metabolic CR proceed to a third cycle and PBSC mobilisation, then ASCT transplant with LEAM conditioning.

- Further management of patients in metabolic PR should be individualised. They may still benefit from ASCT, especially if the Deauville score is 4, hence consider proceeding with a third cycle and PBSC mobilisation, followed by a repeat PET-CT scan with a view to transplant if the quality of response is improved or maintained. Another option is to change to an alternative salvage regimen e.g R-ICE, R-DHAP, noting that only a minority of patients improve their response. Alternatively monitor with further scans, noting that If further progression is demonstrated, the patient may become eligible for CAR-T cell therapy as 3rd line (see 9.5). The second-line IPI, presence of 'double/triple hit' histology, age and fitness and patient's choice should be considered when making this decision.
- Following transplant consolidation RT should be considered, especially if there was only PR prior to transplant.

9.4 Patients with first relapse who are ineligible for both second line CAR-T cell therapy or autologous transplant:

- Factors that should be considered are age and fitness, prior therapy and response, potential suitability for future third line CAR-T cell therapy or anti-CD3 x CD20 bispecific antibody therapy and patient choice.
- Where 3rd line CAR-T cell therapy or anti CD3 x C20 bispecific antibody may be an option, bendamustine should be avoided.
- Otherwise options are glofitamab-GemOx, R-Gem-Ox, or polatuzumab-BR if polatuzumab has not been given with first line therapy.
- For elderly or frail patients consider etoposide-based palliative therapy e.g etoposide +/- steroids, DECC, or RT for local disease and symptom control.

9.5 Second relapse in fit patients < 80 years:

- Offer referral to a CAR-T cell therapy centre at the earliest opportunity.
- Note that patients with CNS disease at second relapse remain eligible for CAR-T cell therapy.
- Alternatively note that patients are also eligible bispecific antibody therapy, i.e glofitamab (if ECOG 0-1), epcoritamab (if ECOG 0-2 and only after prior polatuzumab or where polatuzumab was contraindicated). It remains unclear whether bispecific antibodies or CAR-T cell therapy are superior for this indication.

9.5 Patients with third or later relapse:

- Treatment choice will depend on age, performance status, comorbidity, previous treatments, whether prior CAR-T cell therapy (i.e CD20, CD19 expression, ongoing cytopaenias, toxicities), access to compassionate use programmes and patient choice.
- Fit patients < 80 years of age, should be offered referral to a CAR-T cell therapy centre at the earliest opportunity.
- For young fit patients relapsing after CAR-T cell therapy who have responded to further salvage chemotherapy, consider referral for allogeneic transplantation
- Consider anti CD3 x CD20 bispecific antibody therapy, i.e glofitamab (ECOG score must be 0-1) or epcoritamab (ECOG score must be 0-2, and only if prior polatuzumab or polatuzumab was contra-indicated).

- If CAR-T cell or bispecific antibody therapy are unsuitable options are: R-Gem-Ox, single agent gemcitabine, polatuzumab-BR, loncastuximab (after prior polatuzumab or where polatuzumab was contraindicated) , low dose oral etoposide +/- steroids, DECC, pixantrone, lenalidomide, palliative RT for local disease and symptoms control, or steroids alone.

10.1 Management of relapsed DLBCL with secondary CNS involvement

10.2
- For older patients or those with poor performance status consider pre-phase treatment with once cycle R-HDMTX to improve performances status, then reassess suitability for multi-agent chemotherapy and ASCT.
- Note MATRIX chemotherapy is generally poorly tolerated in older patients > 70 years or younger patients with poor performance status, and is associated with poorer outcomes.
- If receiving MATRIX plan for peripheral blood mobilisation during cycle 2.
- If treated with MATRIX consider 50-75% reduction of cytarabine dose in cycle one for patients > 60 years or with poor performance status.
- Note patients with a with CNS involvement at time of a second relapse are eligible for CAR-T cell therapy and must be referred to a CAR-T centre at the earliest opportunity.
- Note that although relapse with CNS disease is not a specific exclusion with respect to CDF funding for bispecific antibody therapy, these patients were excluded from the pivotal clinical trials.

10.3 Relapse with isolated CNS disease:
- If < 70 years and considered sufficiently fit for high dose therapy options are MATRIX + R-ICE (MARIETTA) regimen, or four cycles MATRIX alone. Repeat MRI brain after two and four cycles. If in CR or good PR offer consolidation with BCNU-thiotepa autologous ASCT.
- If unfit for MATRIX but fit for transplant, i.e generally patients > 70 years, consider two cycles R-MTX-cytarabine (MARTA regimen) followed by BCNU-thiotepa autologous ASCT in responding patients. ADD IT chemo
- Intrathecal methotrexate +/- cytarabine should given if there is leptomeningeal disease until this has cleared.
- If unfit for intensive therapy options are R-HDMTX, whole brain RT or palliative steroids.

10.4 Relapse with concomitant systemic and CNS disease

- Note that outcomes are poor and palliative management may be appropriate for many patients.
- If < 70 years and considered sufficiently fit for high dose therapy offer MATRIX + R-ICE (MARIETTA) regimen. Repeat MRI brain after two and four cycles, and PET-CT after cycle 4. If in CR or good PR offer consolidation with BCNU-thiotepa autologous ASCT.
- If unfit for MATRIX but fit for transplant, i.e generally patients > 70 years, consider two cycles R-MTX-cytarabine (MARTA regimen) and two cycles R-ICE, followed by BCNU-thiotepa autologous ASCT in responding patients.
- Intrathecal methotrexate +/- cytarabine should given if there is leptomeningeal disease until this has cleared

- If unfit for intensive therapy management should be palliative.

11.0 Management of LBCL with 11q aberration

11.1 Note that this diagnosis occurs predominantly in children and young adults. Outcomes appear to be good when treated with intensive chemotherapy as for Burkitt's lymphoma.

11.2 For younger, fit patients <50-60years options are R-CODOX-M-R-IVAC x 2 cycles with intrathecal chemotherapy, or DA-R-EPOCH with intrathecal chemotherapy for older patients.

11.3 If unfit for intensive therapy treatment should be RCHOP +/- HD MTX or intrathecal chemotherapy.

11.3 Management of relapsed and refractory disease should be as for DLBCL. However, note that consolidation with allogeneic SCT may be preferable in this generally younger population. Note also that this group is not eligible for CAR-T cell or bispecific antibody therapy.

12.0 Management of high grade B-cell lymphoma (NOS)

12.1 This entity recognises the fact that there are forms of high grade B-cell lymphoma that resemble Burkitt's lymphoma morphologically but having phenotypic or genotypic features inconsistent with this diagnosis. The clinical behaviour is often more aggressive than DLBCL. Earlier classifications used the term 'B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt's lymphoma'. This should be a rare diagnosis only made when Burkitt's lymphoma and other forms of LBCL have been excluded. It may also include blastoid cases of B-cell lymphoma.

12.2 Note that the optimal therapy for this form is uncertain, there is no standard of care and this must be discussed with the patient.

12.3 Treatment options are RCHOP, polaRCHP, DA R-EPOCH and RCODOX-M/R-IVAC +/- intrathecal therapy depending on clinical and histological and immunophenotypic features, clinical phenotype, presence of or risk of CNS disease, age and fitness.

12.4 Management of relapsed and refractory disease should be as for DLBCL. However, note that consolidation with allogeneic SCT may be preferable in younger patients. Note also that this group is not eligible for CAR-T cell or bispecific antibody therapy.

Appendices:

1 IPI, age-adjusted IPI and NCCN-IPI for diffuse large B-cell lymphoma

One point for each IPI risk factors:

- age > 60yrs
- stage III/IV
- raised LDH
- ECOG >=2
- one site of extranodal disease.

One point for each age-adjusted IPI (more predictive in patients <60ys):

- stage III/IV
- raised LDH
- ECOG ≥2

IPI and age-adjusted IPI

	all ages	age <60yrs
low risk	0-1	0
low-intermediate risk	2	1
high-intermediate risk	3	2
high risk	4-5	3

Overall survival at 5 years according to IPI

	All ages	< 60 yrs
low	73%	83%
low-int	51%	69%
high	43%	46%
high-int	26%	32%

NCCN-IPI

		Score
Age	>40 <60y	1
	>60 ≤ 75y	2
	>75y	3
LDH	>1 ≤ 3 x ULN	1
	>3 x ULN	2
Stage III-IV		1
ECOG ≥2		1
Extranodal		1

*lung, liver, GIT, CNS, marrow

Risk groups		
Score	Risk	5y OS
0-1	Low	96%
2-3	Low-intermediate	82%
4-5	High-intermediate	64%
≥6	High	33%

2 CNS IPI risk score

Risk factors: age >60yr, high LDH, stage III/IV, ECOG score >1, >1 site of extranodal disease, presence of renal/adrenal disease

Risk of CNS relapse at 2 years		
Low	0-1	<1 % risk
Intermediate	2-3	3-4%
High	4-6	10-12%

3 **Second line age adjusted IPI in relapsed diffuse large B-cell lymphoma**

Relapsed DLBCL, all treated with ICE. Age adjusted IPI calculated at initiation of second line therapy

Risk factors: LDH, stage III/IV, performance status (ECOG≥ 2)

Factors		PFS	OS
0	Low	70%	74%
1	Intermediate	39%	49%
2-3	High	16%	18%

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Date: Feb 2026 **Ratified by NSSG:**