Lymphoma Management

HODGKIN LYMPHOMA: Early stage disease has a cure rate of 90% and hence risk adapted combined modality treatment is the current standard of care. PET / PET-CT scans have an active role to play in reducing treatment for early stage disease. Deauville score to be applied, timing of scan is after 2 (or 3) cycles.

1. Early Stage Favourable*: ABVD x 2 to 4 cycles +/- local RT
   If Complete Response after Cycle 2 consider ABVD x 4 cycles
   If Partial Response after Cycle 2 consider ABVD x 4 to 6 cycles→ local RT

2. Early Stage Unfavourable**: ABVD x 4 cycles→ local RT
   If Complete Response after Cycle 2 consider ABVD x 4 cycles→ local RT
   If Partial Response after Cycle 2 consider ABVD x 6 cycles→ local RT

<table>
<thead>
<tr>
<th>Note: EORTC Criteria</th>
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<tr>
<td>Risk Factors: Favourable*: Stage I-II without risk factors</td>
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<tr>
<td>Unfavourable**: Stage I-II with risk factors</td>
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- Bulky Mediastinal mass
- Age > 50 years
- Elevated ESR
- B symptoms
- More than 3 nodal sites

3. Advanced Stage: ABVD x 6 cycles→ +/- local RT to the original bulky disease or post treatment residual disease.
   Elderly patients above the age of 60 years may be treated with COPP instead of ABVD

NON HODGKIN LYMPHOMA - Low Grade (CLL/SLL, FL, MZL)

1. Stage 1 & 2
   Asymptomatic patients can be observed or treated with local RT
   Combined modality chemo-immunotherapy x 3 cycles→ local RT

2. Stage 3 & 4- Asymptomatic
   Observation alone or Single agent Rituximab weekly x 4 followed by Maintenance 2 to 3 monthly for 2 years.

3. Stage 3 & 4- Symptomatic*
   Chemo-immunotherapy x 6 cycles followed by Maintenance Rituximab for 2 years

| Note: Symptomatic* disease is largely based on the BNLI Criteria which include the following: |
| Subjective symptoms, threatened end organ dysfunction, Bulky disease, Cytopenias, disease progressing steadily (doubling time short). |
Choice of regimen should be based on patient age (≤ 65yr or ≥65yrs), co-morbidities. It should be dictated by the local expertise. Common regimens include,

- CVP +/-R
- CHOP+/-R
- Bendamustine+/- R
- In CLL, also consider FCR, Ofatumumab-Chl, Alemtuzumab-Rituximab (high risk CLL).

NON HODGKIN LYMPHOMA- (Common Adult Lymphoma)

**Lymphoblastic Lymphoma (LBL):** Patients with LBL have typically been treated with regimens appropriate for acute lymphoblastic leukaemia (ALL). Cytogenetics and risk stratification is applicable to these patients also. Patients with systemic LBL can be treated with any one of the chemotherapy regimens. For bcr-abl positive patients, a TKI containing protocol must be used.

Young Adults and Adolescent: Use Paediatric ALL Protocols like MCP-841, BFM or MRC-UKALL or COG, etc.

In Older Adults (>40yrs): Use any of the following: GMALL, HyperCVAD, GRALL protocol

**NOTE:**
1. Patients with CR to induction therapy should be continued with other components of the treatment protocols. It is important that patients be treated with a given treatment protocol in its entirety and not be treated with different components taken from different protocols.
2. Patients with high risk features (such as bcr-abl +) and a matched sibling donor should be offered an allogeneic transplantation in first remission.

**Diffuse Large B Cell Lymphoma (DLBCL):** The treatment options vary between patients with localized (stage I-II) and advanced (stage III-IV) disease. Prognosis is extremely good for patients with no adverse risk factors (Normal LDH, stage I or II non-bulky disease, age less than 60 years or ECOG performance status less than 2).

**Stage I-II :** For patients with Non-bulky (<10 cm) stage I or II disease, CHOP +/- Rituximab (R) for 3 cycles with IFRT or 6 cycles of CHOP +/- R alone is recommended (Category 2A).

Patients with bulky disease (10 cm or more) should be treated with 6 cycles of CHOP+/R with or without IFRT (Category 1).

**Stage III-IV:** For patients with advanced stage disease, treatment with 6 cycles of CHOP+/-R repeated every 21 days is recommended (Category 1).

- In selected cases, RT to bulky sites may be beneficial (Category 2B).
- Patients at increased risk of CNS relapse (those with involvement of the paranasal sinuses, testes, breast, bone-marrow involvement with large cells or having two or more extra-
nodal sites with elevated LDH) should receive CNS prophylaxis with 4 doses of Intrathecal methotrexate or 3-3.5 Gm/M² of systemic methotrexate.

**Note:**
1. Patients with bulky disease or impaired renal function should be monitored for tumor lysis syndrome.
2. Hepatitis B reactivation in patients on Rituximab should be discussed and appropriate prophylaxis started.
3. Doxorubicin in CHOP regimen can be replaced with etoposide (CEOP), liposomal doxorubicin or mitoxantrone in patients with poor left ventricular function (Category 2B).
4. Elderly ‘frail’ patients may receive R-mini CHOP.
5. Young patients with Burkitt like lymphomas may be treated with da EPOCH-R.

**Mantle cell lymphoma (MCL)**

**Stage I-II:** Very few patients present with localized low grade MCL. Local RT (30-36Gy) alone or combination chemo-immunotherapy with CHOP-R is recommended (Category 2A).

**Stage II (bulky) and stage III-IV:**

In highly selected patients (low Ki 67) with asymptomatic disease, close observation without any therapy is a reasonable option, especially for those with good performance status and lower IPI.

Aggressive therapies commonly used are CHOP+-/-R alternating with high dose Ara-C based regimens (CHOP-R alternating with DHAP-R x 6 cycles). Other regimens include R-HyperCVAD, R-CHOP / R-ICE, Nordic regimen, CALGB, etc. Choice of the regimen should be based on local expertise and support.

**Note:**
1. For young patients with CR to first line therapy, consolidation with HDT/ASCR is recommended.
2. For patients with PR to first line therapy, second line therapy may be considered in an effort to improve the quality of a response before they are taken for consolidation with HDT/ASCR.

Less aggressive therapies or Bendamustine and Rituximab (B-R x 6 cycles) are recommended for elderly patients, cardiac compromise and patients unfit to tolerate aggressive regimens.

**Maintenance rituximab** is recommended for patients who are not candidates for HDT/ASCR and are in remission after first line therapy with R-CHOP.

**Burkitts Lymphoma (BL):** There is a high incidence of tumour-lysis syndrome and measures should be taken to prevent and treat this complication. Patients with bulky disease and organ dysfunction may be treated with modified dose therapy (e.g. ‘prephase-CVP’), in an attempt to modify the effects of tumor lysis. Then proceed to more intensive therapy as outlined below based on local expertise and supportive care,
Peripheral T - Cell (PTCL) and Anaplastic large cell lymphoma (ALCL): Aggressive T cell lymphoma is divided into two groups:
a. ALK positive ALCL, and
b. PTCL-NoS & others (including ALK negative ALCL).

Treatment with an anthracycline-based chemotherapy regimen – CHOP is recommended.

**Limited stage:** ALCL and no adverse prognostic features by IPI should be treated with 3-4 cycles of CHOP chemotherapy and involved field radiotherapy.

**Advanced Stage:** patients should receive 6-8 cycles of CHOP chemotherapy.

**Note:**
1. ALK-negative ALCL should be treated as for PTCL-NOS
2. There is insufficient data to recommend an alternative regimens like CHOEP, CHOP-14, daEPOCH, Hyper-CVAD in this clinical scenario.
3. Consideration should be given to consolidation with auto-HSCT in the PTCL-NoS group.

NK/T-Cell Lymphoma

**Stage 1 and II:** SMILE x 4 cycles followed by local Radiotherapy is recommended. For patients unable to tolerate intensive chemotherapy Involved field RT is recommended.

**Advanced stage disease** (III and IV) SMILE x 6 cycles followed by Local RT

**Note:** All other subtypes of lymphoma are rare and need to be managed individually as per prevailing guidelines.
**RELAPSED LYMPHOMA**

Histopathological examination is mandatory in the evaluation of relapsed disease. **Management strategy:** A suggested algorithm is as follows

![Algorithm Diagram]

**Chemotherapy regimens for potential candidates for stem cell therapy:** Platinum compound based regimens have been associated with good responses and lower levels of myelotoxicity and are widely used for salvage chemotherapy in potential transplant candidates. These include:

- DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
- ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ± rituximab
- GDP (gemcitabine, dexamethasone, cisplatin) ± rituximab
- ICE (ifosfamide, carboplatin, etoposide) ± rituximab
- MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab
- daEPOCH

**NOTE:**
1. Additional anthracyclines must be used after careful monitoring of the cardiac status.
2. Disease status should be evaluated with imaging studies and clinical assessment after two to three cycles, following which autologous HSCT should be carried out.

**Hematopoietic Stem Cell Transplantation (HSCT):** Commonly used conditioning regimens used in autologous HSCT include

- BCNU, cyclophosphamide, cytosine arabinoside and melphalan (BEAM)
- R-BEAM in B Cell NHL
- Lomustine (CCNU), cytarabine (Ara-C), cyclophosphamide, etoposide (LACE)

**Allogeneic Stem Cell Transplantation**

Allogeneic HSCT may be considered in younger patients with stem cell mobilisation failure or relapse after autologous HSCT that are able to tolerate high dose chemotherapy a second time.

**Chemotherapy regimens in patients who are not candidates for stem cell therapy**

- Clinical trial
- CEPP/PEP C (cyclophosphamide, etoposide, prednisone, procarbazine) ± rituximab
- da-EPOCH ± rituximab
- GDP ± rituximab
- Lenalidomide ± rituximab
- Newer Molecules (compassionate access or if affordable)

**FOLLOW UP**

Patients should be followed up every 3 to 4 monthly for the first 2 years, followed by 6 monthly for the next 3 year and then annually. The following format shall be followed:

1) Accurate history,
2) Careful physical examination,
3) Hematological investigation- CBC, ESR, LDH
4) Documentation of side effects: late effects of treatment,
5) Documentation of 2nd primary,

_Surveillance PET scan has no role in the patient follow up as of date and must be used judiciously._