Primary Mediastinal Large B-Cell Lymphoma

INITIAL EVALUATION

ESSENTIAL:
- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen
- ECOG performance status
- B symptoms (unexplained fever > 38°C during the previous month; recurrent drenching night sweats during the previous month; weight loss > 10% of body weight ≤ 6 months of diagnosis)
- CBC with differential, LDH, BUN, creatinine, albumin, AST, ALT, total bilirubin, alkaline phosphatase, calcium, uric acid
- Beta 2 microglobulin
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBsAg, HCV Ab) (refer to Hepatitis B Virus (HBV) Screening and Management and Hepatitis C Virus (HCV) Screening algorithms)
- PET/CT preferably with contrast
- Calculation of IPI
- MUGA scan or echocardiogram
- Discuss fertility issues and sperm banking for patients of child bearing potential (refer to Fertility Preservation Prior to Cancer Treatment algorithm)
- Lifestyle risk assessment

OF USE IN SELECTED CASES:
- CT neck, chest, abdomen and pelvis with contrast
- CT or MRI of head, and MRI of the spine (only if clinical suspicion of involvement with lymphoma)
- Unilateral or bilateral bone marrow biopsy with or without aspirate
- Pregnancy test
- Consider lumbar puncture and intrathecal chemotherapy if parasinal sinus, testicular, epidural, ≥ 2 extranodal sites, or if IPI score ≥ 3
- Consider thoracentesis if clinically indicated

OF USE IN CERTAIN CIRCUMSTANCES:
- EBER in situ hybridization, LMP-1, HHV-8, CD138, TdT, ALK1
- FISH studies to detect gene rearrangements involving: MYC, BCL2 and/or BCL6
- Molecular studies to detect clonality of the IGH

STONGLY RECOMMENDED:
- FNA or core biopsy for tissue array/banking by protocol

ECOG = Eastern Cooperative Oncology Group

1 Typical immunophenotype: diffuse positivity for CD20 or another pan B-cell marker
2 See Appendix A: International Prognostic Index (IPI)
3 MUGA scan may be omitted for young patients receiving limited anthracycline
4 See Physical Activity, Nutrition, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
Primary Mediastinal Large B-Cell Lymphoma

Note: Consider Clinical Trials as treatment options for eligible patients.

**INDUCTION THERAPY**

- DAEPOCH-R\(^1\) for 6 cycles
- Clinical trial

Evaluate response after 2-3 cycles by PET scan

Patient has greater than or equal to partial response?\(^2\)

- Yes → Continue planned treatment
- No → Core needle or excisional biopsy

Biopsy positive?

- Yes → See Page 3, Post-treatment Response Evaluation
- No → Continue planned treatment

---

1 DAEPOCH-R: dose adjusted EPOCH-R: etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin and rituximab (see Appendix B); administration is based on age and performance status of the patient


Core needle or excisional biopsy

Biopsy positive?

- Yes → See Page 4, Relapse or Refractory Treatment
- No → Continue planned treatment

---

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.
**Primary Mediastinal Large B-Cell Lymphoma**

**Response Evaluation**

- **Complete response**
  - 5PS\(^2\) score 1-3
  - Multidisciplinary conference and/or follow-up evaluation if previous bulky mass\(^1\) or large residual non-fluorodeoxyglucose (FDG) avid mass
  - Complete treatment

- **Partial response**
  - 5PS\(^2\) score 4
  - PET - equivocal\(^4\)
  - Repeat PET scan in 6-8 weeks
  - Consider biopsy of residual mass only if high clinical suspicion or close imaging follow up not feasible
  - Consider Radiation Oncology evaluation
  - PET normalized? (Yes → Complete treatment, No → Biopsy)

- **Biopsy**
  - Biopsy positive? (Yes → See Page 4, Relapse or Refractory Treatment, No → No response or progressive disease)

- **No response or progressive disease**
  - 5PS\(^2\) score 5
  - Multidisciplinary conference and/or consider Radiation Oncology evaluation if:
    - Biopsy or residual mass negative though high clinical/radiographic suspicion
    - Biopsy of residual mass is not possible due to location/patient refusal with high clinical/radiographic suspicion
  - Complete treatment
  - Multidisciplinary conference and/or consider Radiation Oncology evaluation if previous bulky mass\(^2\) or large residual non-FDG avid mass

- **Repeat PET scan in 6-8 weeks**
  - Consider biopsy of residual mass only if high clinical suspicion or close imaging follow up not feasible
  - Consider Radiation Oncology evaluation

- **History and physical with CT neck, chest, abdomen, and pelvis with contrast and labs as clinically indicated:**
  - Every 3 to 4 months for 1 year, then
  - Every 6 months for 2 years, then
  - Annual PA and lateral chest x-ray; consider CT chest with contrast

- **Multidisciplinary conference and/or consider Radiation Oncology evaluation if previous bulky mass\(^2\) or large residual non-FDG avid mass**

- **History and physical with CT neck, chest, abdomen, and pelvis with contrast and labs as clinically indicated:**
  - Every 3 to 4 months for 1 year, then
  - Every 6 months for 2 years, then
  - Annual PA and lateral chest x-ray; consider CT chest with contrast

**Note:** Consider Clinical Trials as treatment options for eligible patients.

---


\(^2\) See Appendix C: 5-Point Scale (5PS)

\(^3\) Bulky disease: mass ≥ 7.5 cm on CT imaging

\(^4\) PET equivocal: maximum standardized uptake value (SUV) greater than mediastinal blood pool in the residual mediastinal mass

---

Copyright 2024 The University of Texas MD Anderson Cancer Center
Primary Mediastinal Large B-Cell Lymphoma

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

Consolidation / ADDITIONAL THERAPY

Relapse or refractory

- Clinical trial
- Standard of care chimeric antigen receptor (CAR) T-cell therapy
- New non cross-resistant regimen chemotherapy (e.g., rituximab with one of the following regimens: ICE, ESHAP, MINE, DHAP) or immunotherapy (e.g., BV-Nivo, pembrolizumab)
- Consider radiation therapy for consolidation with involved site approach
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative

CONsolidation / ADDITIONAL THERAPY

Patient has greater than or equal to partial response?

Yes

- Standard of care CAR T-cell therapy
- High dose therapy plus autologous or allogeneic stem cell transplant if eligible (in the context of a clinical trial)

No

Patient candidate for intensive therapy?

Yes

- Clinical trial
- Standard of care CAR T-cell therapy

No

Individual approach including: clinical trial, palliative chemotherapy or palliative radiation therapy

Note: Consider Clinical Trials as treatment options for eligible patients.

ICE = ifosfamide, carboplatin, etoposide
ESHAP = etoposide, methylprednisolone, high-dose cytarabine, cisplatin
MINE = mesna, ifosfamide, mitoxantrone, etoposide
DHAP = dexamethasone, cytarabine, cisplatin
BV-Nivo = brentuximab vedotin, nivolumab

1 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).


3 Clinical trials or individual regimens: except for patients with disease-free interval, those who progress after three successive regimens are unlikely to derive additional benefit from currently utilized combination chemotherapy regimens.
## APPENDIX A: International Prognostic Index (IPI)

### Pre-Treatment Characteristics, ALL PATIENTS:
- Age > 60 years old
- LDH greater than upper limit of normal
- ECOG performance status 2-4
- Stage III or IV
- Extranodal involvement > 1 site

### International Index, ALL PATIENTS:

<table>
<thead>
<tr>
<th>Number of characteristics</th>
<th>Low</th>
<th>Low intermediate</th>
<th>High intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 or 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Age-Adjusted IPI

### Pre-Treatment Characteristics, ALL PATIENTS ≤ 60 YEARS:
- LDH greater than one times upper limit of normal
- ECOG performance status 2-4
- Extranodal involvement > 1 site

### International Index, ALL PATIENTS ≤ 60 YEARS:

<table>
<thead>
<tr>
<th>Number of characteristics</th>
<th>Low</th>
<th>Low intermediate</th>
<th>High intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX B: Dose Adjusted EPOCH-R

Table 1. EPOCH-R starting dose level

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose, route, treatment days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>375 mg/m² IV Day 1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>50 mg/m²/day continuous IV Days 1-4</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>10 mg/m²/day continuous IV Days 1-4</td>
</tr>
<tr>
<td>Vincristine</td>
<td>0.4 mg/day continuous IV Days 1-4†</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>750 mg/m²/day IV Day 5</td>
</tr>
<tr>
<td>Prednisone</td>
<td>60 mg/m² PO twice daily Days 1-5</td>
</tr>
<tr>
<td>Filgrastim product</td>
<td>5 mcg/kg subcutaneously daily starting on Day 6 until ANC ≥ 5 K/microliter</td>
</tr>
<tr>
<td>Next Cycle**</td>
<td>Day 21</td>
</tr>
</tbody>
</table>

† The original protocol/study dose of vincristine was 0.4 mg/m²/day with no dose cap on vincristine
** Begin on Day 21 if the ANC ≥ 1 K/microliter and the platelet count ≥ 100 K/microliter

Table 2. EPOCH dose-adjustment paradigm

<table>
<thead>
<tr>
<th>Nadir measurements ***</th>
<th>Dose-adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>If nadir ANC ≥ 0.5 K/microliter</td>
<td>20% increase in etoposide, doxorubicin and cyclophosphamide above last cycle</td>
</tr>
<tr>
<td>If nadir ANC &lt; 0.5 K/microliter on 1 or 2 measurements</td>
<td>Same doses as last cycle</td>
</tr>
<tr>
<td>If nadir ANC &lt; 0.5 K/microliter on at least 3 measurements or If nadir platelet count &lt; 25 K/microliter on 1 measurement</td>
<td>20% decrease in etoposide, doxorubicin and cyclophosphamide below last cycle</td>
</tr>
</tbody>
</table>

Note: Dose adjustments above starting dose level apply to etoposide, doxorubicin and cyclophosphamide. Dose adjustments below starting dose level apply to cyclophosphamide only.

*** Measurements of ANC and platelet nadir are based on twice weekly CBC only.
APPENDIX C: 5-Point Scale (5PS)

- Score 1: no uptake
- Score 2: uptake less than or equal to mediastinum
- Score 3: uptake greater than mediastinum but less than or equal to liver
- Score 4: uptake moderately greater than liver
- Score 5: uptake markedly greater than liver and new sites of disease
- Score X: new areas of uptake unlikely to be related to lymphoma

A score of 1-3 is regarded as negative and 4 or 5 as positive.


MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy. Advance Care Planning (ACP) Conversation Workflow (ATT1925)


Continued on next page
SUGGESTED READINGS - continued


Primary Mediastinal Large B-Cell Lymphoma

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center providers at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Core Development Team Leads
Dai Chihara, MD, PhD (Lymphoma/Myeloma)
Chelsea C. Pinnix, MD, PhD (Radiation Oncology)
Jason R. Westin, MD (Lymphoma/Myeloma)

Workgroup Members

Tharakeswara K. Bathala, MBBS, MD (Abdominal Imaging)
Hubert H. Chuang, MD, PhD (Nuclear Medicine)
Bouthaina S. Dabaja, MD (Radiation Oncology)
Luis E. Fayad, MD (Lymphoma/Myeloma)
Olga N. Fleckenstein, BS*
Fredrick B. Hagemeister, MD (Lymphoma/Myeloma)
Benjamin Lee, PharmD, BCPS, BCOP (Pharmacy Clinical Programs)
L. Jeffrey Medeiros, MD (Hematopathology Admin)
Sattva S. Neelapu, MD (Lymphoma/Myeloma)
Chijioke Nze, MD (Lymphoma/Myeloma)
Robert Orlowski, MD, PhD (Lymphoma/Myeloma)
Felipe Samaniego, MD, MPH (Lymphoma/Myeloma)
Nicolaus Wagner-Bartak, MD (Abdominal Imaging)
Michael Wang, MD (Lymphoma/Myeloma)
Mary Lou Warren, DNP, APRN, CNS-CC*
Sireesha Yedururi, MBBS (Abdominal Imaging)

*Clinical Effectiveness Development Team