NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:
Diffuse Large B-cell Lymphoma (Part 1 of 4)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment. Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced health care team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies. These Guidelines are a work in progress that may be refined as often as new significant data become available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Systemic Therapy for Diffuse Large B-cell Lymphoma

Note: All recommendations are Category 2A unless otherwise indicated.

**First-line Therapy**

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
</table>
| R-CHOP (Category 1) | Days 1, 22, and 43: Rituximab 375mg/m² IV 7 days prior to beginning CHOP regimen  
Day 1: Cyclophosphamide 750mg/m² IV + doxorubicin 50mg/m² IV bolus + vincristine 1.4mg/m² IV bolus (max dose 2mg)  
Days 3, 4, 24, and 45: Prednisone 100mg orally 5 days. Repeat each cycle every 3 weeks for 3 cycles. Radiotherapy begins 3 weeks after last cycle of R-CHOP. |
| Dose-dense R-CHOP 14 (Category 3) | Day 1: Cyclophosphamide 750mg/m² IV + doxorubicin 50mg/m² IV + vincristine 2mg IV  
Days 1-5: Prednisone 100mg orally. Repeat every 2 weeks for 6 cycles. Granulocyte colony-stimulating factor (G-CSF) was given on day 4 or 6. |
| Dose-adjusted EPOCH + rituximab (Category 2B) | Day 1: Rituximab 375mg/m² IV  
Days 1–4: Etoposide 50mg/m² IV + doxorubicin 10mg/m² IV + vincristine 0.4mg/m² IV  
Day 5: Cyclophosphamide 750mg/m² IV  
Days 1–5: Prednisone 60mg/m² orally twice daily. Administer G-CSF 5 mcg/kg SQ daily until an ANC >5 × 10⁹/L above nadir level starting day 6. Repeat cycle every 3 weeks for 6 cycles. |

**First-line Therapy for Patients With Poor Left Ventricular Function or Very Frail**

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
</table>
| RCEPP10 | Days 1 and 8: Cyclophosphamide 600mg/m² IV  
Day 1: Etoposide 70mg/m² IV (or days 1–3 if not giving oral etoposide)  
Days 2 and 3: Etoposide 140 mg/m² orally (rounded to the nearest 50mg capsule)  
Days 1–10: Procarbazine 60mg/m² orally + prednisone 60mg/m² orally. Repeat every 28 days until disease progression, or unacceptable toxicity. |
| RCDOP11,12 | Day 1: Cyclophosphamide 750mg/m² IV + liposomal doxorubicin 30mg/m² IV + vincristine 2mg IV  
Days 1–5: Prednisone 60mg/m² IV  
Day 8: Rituximab 375mg/m² IV for cycle 1; administer on day 0 in subsequent cycles. Repeat cycle every 3 weeks for 6–8 cycles. |
| RGCVP13 | Day 1: Rituximab 375mg/m² IV + cyclophosphamide 750mg/m² IV + vincristine 1.4mg/m² (maximum dose 2mg) IV  
Days 1 and 8: Gemcitabine 750-1000mg/m² IV  
Days 1–5: Prednisolone 100mg orally per day.  
Day 9: Pegfilgrastim 6mg SC. Repeat every 3 weeks for 6 cycles (Patients considered high risk for CNS relapse can receive methotrexate 12.5mg IT for 3 cycles). |
| DA-EPOCH + rituximab14 | Day 1: Rituximab 275mg/m²  
Days 1–4: Doxorubicin 10mg/m² IV + etoposide 50mg/m² IV + vincristine 0.4mg/m² IV  
Day 5: Cyclophosphamide 750mg/m² IV  
Days 1–5: Prednisone 60mg/m² orally. Administer G-CSF on day 6 until ANC exceeds nadir. Repeat cycle every 3 weeks. |
| RCEOP15 | Day 1: Rituximab 375mg/m² IV  
Day 1: Cyclophosphamide 750mg/m² IV + etoposide 50mg/m² IV + vincristine 1.4mg/m² IV (max dose 2mg)  
Days 1–5: Prednisone 100mg orally  
Days 2–3: Etoposide 100mg/m² orally. For limited-stage disease, repeat cycle every 3 weeks for 3–4 cycles; for advanced-stage disease, repeat cycle every 3 weeks for 6 cycles. |

continued
## Systemic Therapy for Diffuse Large B-cell Lymphoma (continued)

### Patients >80 Years of Age With Comorbidities

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
</table>
| R-mini-CHOP 16 | Day 1: Rituximab 375mg/m² IV  
Day 1: Cyclophosphamide 400mg/m² IV + doxorubicin 25mg/m² IV + vincristine 1mg IV  
Days 1–5: Prednisone 40mg/m² orally.  
Repeat every 3 weeks for 6 cycles. |
| RGCV 13 | Day 1: Rituximab 375mg/m² IV + cyclophosphamide 750mg/m² IV + vincristine 1.4mg/m² (maximum dose 2mg) IV  
Days 1 and 8: Gemcitabine 750-1000mg/m² IV  
Days 1–5: Prednisolone 100mg orally per day  
Day 9: Pegfilgrastim 6mg SC.  
Repeat every 3 weeks for 6 cycles (Patients considered high risk for CNS relapse can receive methotrexate 12.5mg IT for 3 cycles). |

### First-line Consolidation (optional)

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-dose therapy with autologous stem cell rescue in patients with age-adjusted IPI high-risk disease (Category 2B) 17</td>
<td>Induced with 5 cycles of CHOP or R-CHOP followed by autotransplantation at the first response to induction therapy with CHOP with or without rituximab for 3 cycles.</td>
</tr>
<tr>
<td>High-dose therapy with autologous stem cell rescue in patients with double-hit DLBCL 17</td>
<td>Induced with 5 cycles of CHOP or R-CHOP followed by autotransplantation at the first response to induction therapy with CHOP with or without rituximab for 3 cycles.</td>
</tr>
</tbody>
</table>

### Concurrent Presentation With CNS Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenchymal 1</td>
<td>Systemic methotrexate 3g/m² or more on day 15 of a 21-day R-CHOP cycle that has been supported by growth factors.</td>
</tr>
<tr>
<td>Leptomeningeal 1</td>
<td>Methotrexate/cytarabine IT. Consider Ommaya reservoir placement and/or systemic methotrexate 3-3.5g/m².</td>
</tr>
</tbody>
</table>

### Second-line Therapy (for patients with intention to proceed to high-dose therapy)

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
</tr>
</thead>
</table>
| DHAP ± rituximab 18–20 | Days 1–4: Cisplatin 100mg/m² IV via 24-hour infusion + cytosine 2g/m² in 2 pulses each given 12 hours apart IV + dexamethasone 40mg orally or IV ± rituximab 375mg/m² IV prior to DHAP.  
Repeat in 3–4 weeks for 6-10 cycles. |
| ESHAP ± rituximab 21,22 | Days 1–4: Etoposide 40–60mg/m²  
Days 1–5: Methylprednisolone 250–500mg IV  
Day 5: Cytarabine 2g/m² IV over 2–3 hours  
Days 1–4: Cisplatin 25mg/m² IV via 24-hour infusion, ±  
Day 1 or 5: Rituximab 375mg/m² IV.  
Repeat every 3–4 weeks for 3 cycles. |
| GDP ± rituximab 23,24 | Days 1 and 8: Gemcitabine 1000mg/m² IV over 30 minutes  
Days 1–4: Dexamethasone 40mg orally  
Day 1: Cisplatin 75mg/m² IV OR carboplatin at AUC 5mg·min/mL IV over 30 minutes, ±  
Day 8: Rituximab 375mg/m² slow IV infusion for CD20-positive disease.  
Repeat every 3 weeks for up to 6 cycles. |
| GemOX ± rituximab 25 | Day 1: Gemcitabine 1000mg/m² and oxaliplatin 100mg/m² ± rituximab 375mg/m² IV.  
Repeat every 15 days if ANC >1 × 10⁹/L and platelet count >100 × 10⁹/L; if not, then every 3 weeks. |
| ICE ± rituximab 26–28 | Days 1–3: Etoposide 100mg/m² IV bolus  
Day 2: Carboplatin AUC 5mg·min/mL (max dose 800mg) IV bolus and ifosfamide admixed with mesna both at a dose of 5g/m² via 24-hour continuous IV beginning day 2  
Days 5–12 (or days 7–14): Filgrastim 5mg/kg/day for cycles 1–2, increased to 10mg/kg/day following cycle 3 until completion of peripheral blood stem cell collection, ±  
Days 1 and 3: Rituximab 375mg/m² IV and on cycle 1, give additional dose rituximab 375mg/m² on Day 2.  
Repeat every 14 days or when ANC >1000 cells/mL and platelet count >50000/mL. |
| MINE ± rituximab 29,30c | Day 1: Mitoxantrone 8mg/m² IV  
Days 1–3: Ifosfamide 2g/m² IV + mesna IV + etoposide 100mg/m² IV, ±  
Day 1: Rituximab 375mg/m² IV.  
Repeat cycle every 4 weeks for 2 cycles, followed by high-dose chemotherapy and autologous stem cell transplantation (HDC-ASCT). Patients in remission after HDC-ASCT may receive rituximab 375mg/m² IV weekly for 4 weeks. |
### Systemic Therapy for Diffuse Large B-cell Lymphoma1 (continued)

#### Second-line Therapy (non-candidates for high-dose therapy)

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOsinG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bendamustine ± rituximab</strong>&lt;sup&gt;11-33d&lt;/sup&gt;</td>
<td><strong>Days 1–2</strong>: Bendamustine 120mg/m² IV, ± Rituximab 375mg/m² IV. Repeat every 21 days for 2–6 cycles.</td>
</tr>
<tr>
<td><strong>Brentuximab vedotin for CD30+ disease (Category 2B)</strong>&lt;sup&gt;34&lt;/sup&gt;</td>
<td>Brentuximab vedotin 1.8mg/kg IV over 30 minutes every 3 weeks. Repeat cycle until a maximum of 16 cycles, disease progression, or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>CEOP ± rituximab</strong>&lt;sup&gt;(PO and IV)&lt;/sup&gt;&lt;sup&gt;10&lt;/sup&gt;</td>
<td><strong>Days 1 and 8</strong>: Cyclophosphamide 600mg/m² IV Day 1: Etoposide 70mg/m² IV (or on days 1–3 if not giving oral etoposide) <strong>Days 2 and 3</strong>: Etoposide 140mg/m² orally (rounded to the nearest 50 mg capsule) <strong>Days 1–10</strong>: Procarbazine 60mg/m² orally + prednisone 60mg/m² orally, ± Rituximab 375mg/m² IV. Repeat every 28 days until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>CEPP ± rituximab</strong>&lt;sup&gt;(PO and IV)&lt;/sup&gt;&lt;sup&gt;34&lt;/sup&gt;</td>
<td><strong>Days 1</strong>: Cyclophosphamide 750mg/m² IV, vincristine 1.4mg/m² IV, and epirubicin 60mg/m² IV <strong>Days 1–5</strong>: Prednisone 100mg/day orally, ± Rituximab 375mg/m² IV. Repeat every 3 weeks for at least 6 cycles.</td>
</tr>
<tr>
<td><strong>DA-EPOCH ± rituximab</strong>&lt;sup&gt;36,37&lt;/sup&gt;</td>
<td><strong>Days 2–4</strong>: Doxorubicin 15mg/m² via continuous IV infusion + etoposide 65mg/m² via continuous IV infusion + vincristine 0.5mg via continuous IV infusion <strong>Day 5</strong>: Cyclophosphamide 750mg/m² IV <strong>Days 1–14</strong>: Prednisone 60mg/m² orally, ± Rituximab 375mg/m²/m² IV. Repeat every 21 days for 4–6 cycles.</td>
</tr>
<tr>
<td><strong>GDP ± rituximab</strong>&lt;sup&gt;38,39&lt;/sup&gt;</td>
<td><strong>Days 1 and 8</strong>: Gemcitabine 1000mg/m² IV <strong>Days 1–4</strong>: Dexamethasone 40mg IV <strong>Days 1–3</strong>: Cisplatin 25mg/m² IV OR carboplatin AUC 5mg/min/ML on day 1, ± Rituximab 375mg/m² IV. Repeat every 21 days for 2–6 cycles (max of 4 cycles if using carboplatin).</td>
</tr>
<tr>
<td><strong>GemOx ± rituximab</strong>&lt;sup&gt;40,41&lt;/sup&gt;</td>
<td><strong>Days 1 and 8</strong>: Gemcitabine 1200mg/m² 30-minute IV infusion <strong>Day 2</strong>: Oxaliplatin 120mg/m² 2-hour IV infusion, ± Rituximab 375mg/m² IV. Repeat every 21 days for 6 cycles.</td>
</tr>
<tr>
<td><strong>Lenalidomide ± rituximab</strong>&lt;sup&gt;(non-GCB DLBCL)&lt;/sup&gt;&lt;sup&gt;42-44&lt;/sup&gt;</td>
<td><strong>Days 1–21</strong>: Lenalidomide 20mg orally ± rituximab 375mg/m² IV weekly during cycle 1. Repeat every 28 days until complete response.</td>
</tr>
<tr>
<td><strong>Rituximab</strong>&lt;sup&gt;45&lt;/sup&gt;</td>
<td><strong>Day 1</strong>: Rituximab 375mg/m² IV during each cycle of chemotherapy for up to 8 infusions.</td>
</tr>
</tbody>
</table>

---

**References**


---

continued
NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Diffuse Large B-cell Lymphoma (Part 4 of 4)

References


