

## NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Diffuse Large B-Cell Lymphoma (Part 1 of 5)

**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 healthcare 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 only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes 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<sup>1</sup>

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

#### First-Line Therapy

REGIMEN	DOSING
<b>R-CHOP (category 1)<sup>2-4</sup></b>	<p><b>Days 1, 22, and 43:</b> Rituximab 375mg/m<sup>2</sup> IV 7 days prior to beginning CHOP regimen</p> <p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV, doxorubicin 50mg/m<sup>2</sup> IV bolus, and vincristine 1.4mg/m<sup>2</sup> IV bolus (max dose 2mg)</p> <p><b>Days 3, 24, and 45:</b> Prednisone 100mg PO 5 days</p> <p>Repeat each cycle every 3 weeks for 3 cycles. Radiotherapy begins 3 weeks after last cycle of R-CHOP.</p>
<b>Dose-dense R-CHOP 14 (category 3)<sup>5,6</sup></b>	<p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV, doxorubicin 50mg/m<sup>2</sup> IV, and vincristine 2mg IV</p> <p><b>Days 1-5:</b> Prednisone 100mg PO</p> <p>Repeat every 2 weeks for 6 cycles. Granulocyte colony-stimulating factor (G-CSF) was given on day 4 or 6.</p>
<b>Dose-adjusted EPOCH + rituximab (category 2B)<sup>7-9</sup></b>	<p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV day 1</p> <p><b>Days 1-4:</b> Etoposide 50mg/m<sup>2</sup> IV, doxorubicin 10mg/m<sup>2</sup>, and vincristine 0.4mg/m<sup>2</sup></p> <p><b>Day 5:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> PO BID</p> <p>Administer G-CSF 5 mcg/kg SQ daily until an ANC &gt;5 × 10<sup>9</sup>/L above nadir level starting day 6. Repeat cycle every 3 weeks for 6 cycles.</p>

#### First-Line Therapy for Patients with Poor Left Ventricular Function or Very Frail<sup>10</sup>

<b>RCEPP<sup>10</sup></b>	<p><b>Days 1 and 8:</b> Cyclophosphamide 600mg/m<sup>2</sup> IV</p> <p><b>Day 1:</b> Etoposide IV 70mg/m<sup>2</sup> IV (or days 1-3 if not giving PO etoposide)</p> <p><b>Days 2 and 3:</b> Etoposide 140 mg/m<sup>2</sup> PO (rounded to the nearest 50mg capsule)</p> <p><b>Days 1-10:</b> Procarbazine 60mg/m<sup>2</sup> PO and prednisone 60mg/m<sup>2</sup> PO</p> <p>Repeat every 28 days until disease progression, or unacceptable toxicity.</p>
<b>RCDOP<sup>11, 12</sup></b>	<p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV, liposomal doxorubicin 30mg/m<sup>2</sup> IV, and vincristine 2mg IV</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> IV</p> <p><b>Day 8:</b> Rituximab 375mg/m<sup>2</sup> IV for cycle 1; administer on day 0 in subsequent cycles</p> <p>Repeat cycle every 3 weeks for 6-8 cycles.</p>
<b>RCNOP<sup>13-15</sup></b>	<p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV</p> <p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV, mitoxantrone 10mg/m<sup>2</sup> IV, and vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg)</p> <p><b>Days 1-5:</b> Prednisone 50mg/m<sup>2</sup> PO</p> <p>Repeat cycle every 3 weeks for 6 cycles (max 8 cycles).</p>
<b>DA-EPOCH + rituximab<sup>16</sup></b>	<p><b>Day 1:</b> Rituximab 275mg/m<sup>2</sup></p> <p><b>Days 1-4:</b> Doxorubicin 10mg/m<sup>2</sup> IV, etoposide 50mg/m<sup>2</sup> IV, and vincristine 0.4mg/m<sup>2</sup> IV</p> <p><b>Day 5:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> PO</p> <p>Administer G-SCF on day 6 until ANC exceeds nadir; repeat cycle every 3 weeks.</p>
<b>RCEOP<sup>17</sup></b>	<p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV</p> <p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV, etoposide 50mg/m<sup>2</sup> IV, and vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg)</p> <p><b>Days 1-5:</b> Prednisone 100mg PO</p> <p><b>Days 2-3:</b> Etoposide 100mg/m<sup>2</sup> PO</p> <p>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.</p>

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## NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Diffuse Large B-Cell Lymphoma (Part 2 of 5)

### Systemic Therapy for Diffuse Large B-cell Lymphoma<sup>1</sup> (continued)

#### Patients >80 Years of Age with Comorbidities

REGIMEN	DOSING
<b>R-mini-CHOP<sup>18</sup></b>	<p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup></p> <p><b>Day 1:</b> Cyclophosphamide 400mg/m<sup>2</sup>, doxorubicin 25mg/m<sup>2</sup>, and vincristine 1mg</p> <p><b>Days 1-5:</b> Prednisone 40mg/m<sup>2</sup></p> <p>Repeat every 3 weeks for 6 cycles.</p>

#### First-Line Consolidation (optional)

<b>High-dose therapy with autologous stem cell rescue in patients with age-adjusted IPI high-risk disease (category 2b)<sup>19</sup></b>	Induced with 5 cycles of CHOP or R-CHOP <b>followed by</b> autotransplantation at the first response to induction therapy with CHOP with or without rituximab for 3 cycles
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#### Concurrent Presentation with CNS Disease

<b>Parenchymal<sup>1</sup></b>	Systemic methotrexate 3g/m <sup>2</sup> or more on day 15 of a 21-day R-CHOP cycle that has been supported by growth factors.
<b>Leptomeningeal<sup>1</sup></b>	Methotrexate/cytarabine IT.

#### Second-Line Therapy (for patients with intention to proceed to high-dose therapy with autologous stem cell rescue)

<b>DHAP + rituximab<sup>20-22</sup></b>	<p><b>Days 1-4:</b> Cisplatin 100mg/m<sup>2</sup> IV via 24-hour infusion, cytosine 2g/m<sup>2</sup> in 2 pulses each given 12 hours apart, and dexamethasone 40mg PO or IV <b>plus</b> rituximab 375mg/m<sup>2</sup> IV prior to DHAP</p> <p>Repeat in 3-4 weeks for 6-10 cycles.</p>
<b>ESHAP + rituximab<sup>23,24</sup></b>	<p><b>Days 1-4:</b> Etoposide 40-60mg/m<sup>2</sup></p> <p><b>Days 1-5:</b> Methylprednisolone 250-500mg IV</p> <p><b>Day 5:</b> Cytarabine 2g/m<sup>2</sup> IV over 2-3 hours</p> <p><b>Days 1-4:</b> Cisplatin 25mg/m<sup>2</sup> IV via 24-hour infusion</p> <p><b>Day 1 or 5:</b> Rituximab 375mg/m<sup>2</sup> IV</p> <p>Repeat every 3-4 weeks for 3 cycles.</p>
<b>GDP + rituximab<sup>25,26</sup></b>	<p><b>Days 1 and 8:</b> Gemcitabine 1000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-4:</b> Dexamethasone 40mg PO</p> <p><b>Day 1:</b> Cisplatin 75mg/m<sup>2</sup> IV OR carboplatin at AUC = 5 IV over 30 min</p> <p><b>Day 8:</b> Rituximab 375mg/m<sup>2</sup> slow IV infusion for CD20-positive disease</p> <p>Repeat every 3 weeks for up to 6 cycles.</p>
<b>GEMOX + rituximab<sup>27</sup></b>	<p><b>Day 1:</b> Gemcitabine 1000mg/m<sup>2</sup> and oxaliplatin 100mg/m<sup>2</sup> <b>plus</b> rituximab 375mg/m<sup>2</sup></p> <p>Repeat every 15 days if ANC &gt;1 × 10<sup>9</sup>/L and platelet count &gt;100 × 10<sup>9</sup>/L; if not, then every 3 weeks.</p>
<b>ICE + rituximab<sup>28-30</sup></b>	<p><b>Days 1-3:</b> Etoposide 100mg/m<sup>2</sup> IV bolus</p> <p><b>Day 2:</b> Carboplatin AUC = 5 (max dose 800mg) IV bolus and ifosfamide admixed with mesna both at a dose of 5g/m<sup>2</sup> via 24-hour continuous IV beginning day 2</p> <p><b>Days 1 and 3:</b> Rituximab 375mg/m<sup>2</sup> IV bolus and on cycle 1, give additional dose rituximab 375mg/m<sup>2</sup> on day 2</p> <p><b>Days 5-12 (or days 7-14):</b> Filgrastim 5mcg/kg/day for cycles 1-2, increased to 10mcg/kg/day following cycle 3 until completion of peripheral blood stem cell collection</p> <p>Repeat every 14 days or when ANC &gt;1000 cells/mcL and platelet count &gt;50000/mcL.</p>
<b>MINE + rituximab<sup>31,32†</sup></b>	<p><b>Days 1-3:</b> Mesna 13g/m<sup>2</sup> and ifosfamide 1.3g/m<sup>2</sup></p> <p><b>Day 1:</b> Mitoxantrone 12mg/m<sup>2</sup></p> <p><b>Days 1-3:</b> Etoposide 65mg/m<sup>2</sup></p> <p><b>Days 1, 6, and 8:</b> Rituximab 400mg/m<sup>2</sup> for 3 weeks</p> <p>Repeat every 3 weeks for 2 cycles.</p>

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

<b>Bendamustine + rituximab<sup>33-35§</sup></b>	<p><b>Days 1-2:</b> Bendamustine 120mg/m<sup>2</sup></p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup></p> <p>Repeat every 28 days for up to 6 cycles.</p>
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# NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Diffuse Large B-Cell Lymphoma (Part 3 of 5)

## Systemic Therapy for Diffuse Large B-cell Lymphoma<sup>1</sup> (continued)

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

REGIMEN	DOSING
<b>CEPP + rituximab (PO and IV)<sup>10</sup></b>	<b>Days 1 and 8:</b> Cyclophosphamide 600mg/m <sup>2</sup> IV <b>Day 1:</b> Etoposide IV 70mg/m <sup>2</sup> IV (or on days 1–3 if not giving PO etoposide) <b>Days 2 and 3:</b> Etoposide 140mg/m <sup>2</sup> PO (rounded to the nearest 50 mg capsule) <b>Days 1–10:</b> Procarbazine 60mg/m <sup>2</sup> PO and prednisone 60mg/m <sup>2</sup> PO Repeat every 28 days until disease progression or unacceptable toxicity.
<b>CEOP + rituximab<sup>36</sup></b>	<b>Day 1:</b> Cyclophosphamide 750mg/m <sup>2</sup> IV, vincristine 1.4mg/m <sup>2</sup> IV, and epirubicin 60mg/m <sup>2</sup> IV <b>Days 1–5:</b> Prednisone 100mg/day PO <b>Day 0:</b> Rituximab 375mg/m <sup>2</sup> Repeat every 3 weeks for at least 6 cycles.
<b>DA-EPOCH + rituximab<sup>37,38</sup></b>	<b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV <b>Days 2–4:</b> Doxorubicin 15mg/m <sup>2</sup> via continuous IV infusion, etoposide 65mg/m <sup>2</sup> via continuous IV infusion, and vincristine 0.5mg via continuous IV infusion <b>Day 5:</b> Cyclophosphamide 750mg/m <sup>2</sup> IV <b>Days 1–14:</b> Prednisone 60mg/m <sup>2</sup> PO Repeat every 21 days for 4–6 cycles.
<b>GDP + rituximab<sup>39,40</sup></b>	<b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV <b>Days 1 and 8:</b> Gemcitabine 1000mg/m <sup>2</sup> IV <b>Days 1–4:</b> Dexamethasone 40mg IV <b>Days 1–3:</b> Cisplatin 25mg/m <sup>2</sup> IV <b>OR</b> carboplatin AUC = 5 on day 1 Repeat every 21 days for 2–6 cycles (max of 4 cycles if using carboplatin).
<b>GemOx + rituximab<sup>41,42</sup></b>	<b>Days 1 and 8:</b> Gemcitabine 1200mg/m <sup>2</sup> 30-minute IV infusion <b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> <b>Day 2:</b> Oxaliplatin 120mg/m <sup>2</sup> 2-hour IV infusion Repeat every 21 days for 6 cycles.
<b>Lenalidomide + rituximab<sup>43–45</sup></b>	<b>Days 1–21:</b> Lenalidomide 20mg PO plus rituximab 375mg/m <sup>2</sup> IV weekly during cycle 1 Repeat every 28 days until complete response.
<b>Rituximab<sup>46</sup></b>	<b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV during each cycle of chemotherapy for up to 8 infusions

\* Inclusion of any anthracycline or anthracenedione in patients with impaired cardiac functioning should have more frequent cardiac monitoring.

† There are limited published data regarding the use of these regimens; however, they are used at NCCN Member Institutions for the first-line treatment of DLBCL for patients with poor left ventricular function.

‡ Used in patients receiving consolidation treatment following CHOP in those achieving complete response or near-complete response.

§ Preferred for elderly patients.

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